

<http://www.cas.org/legal/infopolicy.html>

This file contains CAS Registry Numbers for easy and accurate substance identification.

=> e kase hiroshi/au

E1	9	KASE HIROMI/AU
E2	3	KASE HIROMITSU/AU
E3	236 -->	KASE HIROSHI/AU
E4	1	KASE HIROTOSHI/AU
E5	47	KASE HIROYUKI/AU
E6	1	KASE HISAYUKI/AU
E7	2	KASE HITOMI/AU
E8	1	KASE IKUKO/AU
E9	21	KASE J/AU
E10	1	KASE JASON/AU
E11	3	KASE JASON P/AU
E12	1	KASE JOHANNA/AU

=> s e3

L1 236 "KASE HIROSHI"/AU

=> s l1 and xanthin?

24194 XANTHIN?

L2 13 L1 AND XANTHIN?

=> d l2 ibib abs ti hit 1-5

L2 ANSWER 1 OF 13 CAPLUS COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 2005:1103616 CAPLUS Full-text

DOCUMENT NUMBER: 143:373375

TITLE: Preventive and/or therapeutic agent for disease

INVENTOR(S): accompanied by chronic muscle/skeleton pain  
Kase, Hiroshi; Takahashi, Isami; Kunori, Shunji; Kobayashi, Minoru; Shiozaki, Shizuo; Shirakura, Shiro

PATENT ASSIGNEE(S): Kyowa Hakko Kogyo Co., Ltd., Japan

SOURCE: PCT Int. Appl., 48 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: Japanese

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
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WO 2005094885	A1	20051013	WO 2005-JP6033	
20050330				
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ,			

NA, NI,  
NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK,  
SL, SM,  
SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU,  
ZA, ZM, ZW  
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM,  
ZW, AM,  
AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ,  
DE, DK,  
EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL,  
PL, PT,  
RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ,  
GW, ML,

MR, NE, SN, TD, TG  
CA 2561383 A1 20051013 CA 2005-2561383  
20050330  
EP 1738766 A1 20070103 EP 2005-727903  
20050330  
R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR,  
HU, IE,  
IS, IT, LI, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR,  
AL, BA,  
HR, LV, MK, YU  
US 20070149555 A1 20070628 US 2006-594684  
20060928  
PRIORITY APPLN. INFO.: JP 2004-97422 A  
20040330  
WO 2005-JP6033 W

20050330  
OTHER SOURCE(S): MARPAT 143:373375  
AB A preventive and/or therapeutic agent for diseases accompanied by  
a chronic muscle/skeleton pain contains xanthine derivs. or salts  
thereof having antagonistic activity against an adenosine A2A  
receptor. For example, 8-[2-(3,4-dimethoxyphenyl)ethenyl]-1,3-  
diethyl-3,7-dihydro-7- methyl-1H-purine-2,6-dione was tested for  
pain-relieving effects among rat models with musculoskeletal pain.  
Formulations for tablets, capsules, and injections were also  
provided.  
TI Preventive and/or therapeutic agent for disease accompanied by  
chronic  
muscle/skeleton pain  
REFERENCE COUNT: 16 THERE ARE 16 CITED REFERENCES AVAILABLE  
FOR THIS

RECORD. ALL CITATIONS AVAILABLE IN THE  
RE FORMAT  
IN Kase, Hiroshi; Takahashi, Isami; Kunori, Shunji; Kobayashi,  
Minoru; Shiozaki, Shizuo; Shirakura, Shiro  
AB A preventive and/or therapeutic agent for diseases accompanied by  
a chronic muscle/skeleton pain contains xanthine derivs. or salts  
thereof having antagonistic activity against an adenosine A2A  
receptor. For example, 8-[2-(3,4-dimethoxyphenyl)ethenyl]-1,3-  
diethyl-3,7-dihydro-7- methyl-1H-purine-2,6-dione was tested for  
pain-relieving effects among rat models with musculoskeletal pain.  
Formulations for tablets, capsules, and injections were also  
provided.  
ST xanthine deriv musculoskeletal pain treatment  
IT Adenosine receptors

RL: BSU (Biological study, unclassified); BIOL (Biological study)  
 (A2A, antagonists; xanthine derivs. as therapeutic agents for  
 disease accompanied by chronic muscle/skeleton pain)  
 IT Drug delivery systems  
 (capsules; xanthine derivs. as therapeutic agents for disease  
 accompanied by chronic muscle/skeleton pain)  
 IT Fatigue, biological  
 (chronic fatigue syndrome; xanthine derivs. as therapeutic  
 agents for disease accompanied by chronic muscle/skeleton pain)  
 IT Musculoskeletal diseases  
 (chronic pain; xanthine derivs. as therapeutic agents for  
 disease accompanied by chronic muscle/skeleton pain)  
 IT Lyme disease  
 (fibromyalgia from; xanthine derivs. as therapeutic agents  
 for disease accompanied by chronic muscle/skeleton pain)  
 IT Muscle, disease  
 (fibromyalgia; xanthine derivs. as therapeutic agents for  
 disease accompanied by chronic muscle/skeleton pain)  
 IT Muscle, disease  
 (fibrositis; xanthine derivs. as therapeutic agents for  
 disease accompanied by chronic muscle/skeleton pain)  
 IT Muscle, disease  
 (generalized tendomyopathy; xanthine derivs. as therapeutic  
 agents for disease accompanied by chronic muscle/skeleton pain)  
 IT Drug delivery systems  
 (injections; xanthine derivs. as therapeutic agents for  
 disease accompanied by chronic muscle/skeleton pain)  
 IT Muscle, disease  
 Pain  
 (myalgia; xanthine derivs. as therapeutic agents for disease  
 accompanied by chronic muscle/skeleton pain)  
 IT Drug delivery systems  
 (tablets; xanthine derivs. as therapeutic agents for disease  
 accompanied by chronic muscle/skeleton pain)  
 IT Disease, animal  
 (temporomandibular joint; xanthine derivs. as therapeutic  
 agents for disease accompanied by chronic muscle/skeleton pain)  
 IT Joint, anatomical  
 (temporomandibular, disease; xanthine derivs. as therapeutic  
 agents for disease accompanied by chronic muscle/skeleton pain)  
 IT Rheumatic diseases  
 Rheumatoid arthritis  
 (xanthine derivs. as therapeutic agents for disease  
 accompanied by chronic muscle/skeleton pain)  
 IT 31377-36-3 149744-74-1 861387-30-6 861387-31-7  
 RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL  
 (Biological study); USES (Uses)  
 (xanthine derivs. as therapeutic agents for disease  
 accompanied by chronic muscle/skeleton pain)

L2 ANSWER 2 OF 13 CAPLUS COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 2005:729536 CAPLUS Full-text

DOCUMENT NUMBER: 143:166695

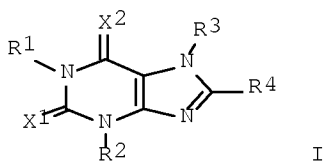
TITLE: Drug for treating migraine

INVENTOR(S): Takeuchi, Megumi; Takayama, Makoto; Shirakura,  
 Shiro;

Kase, Hiroshi

PATENT ASSIGNEE(S): Kyowa Hakko Kogyo Co., Ltd., Japan  
 SOURCE: PCT Int. Appl., 21 pp.  
 CODEN: PIXXD2  
 DOCUMENT TYPE: Patent  
 LANGUAGE: Japanese  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005072739	A1	20050811	WO 2005-JP1634	
20050128				
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, MR, NE, SN, TD, TG				
CA 2554426	A1	20050811	CA 2005-2554426	
20050128				
EP 1709967	A1	20061011	EP 2005-704394	
20050128				
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, FI, RO, CY, TR, BG, CZ, EE, HU, PL, SK, IS				
US 20070161663	A1	20070712	US 2006-587264	
20060911				
PRIORITY APPLN. INFO.:			JP 2004-19496	A
20040128				
			WO 2005-JP1634	W
20050128				
OTHER SOURCE(S):			MARPAT 143:166695	
GI				



AB Disclosed is a drug for treating migraine which contains, as an active constituent, a xanthine derivative represented by the formula (I) below or a pharmacol. acceptable salt thereof. (In the formulas, I; R1, R2 and R3 may be the same or different and resp. represent a hydrogen atom, a lower alkyl, a lower alkenyl or a lower alkynyl; R4 represents a cycloalkyl,  $-(CH_2)_n-R_5$  or one represented by the above formula (II); and X1 and X2 may be the same or different and resp. represent an oxygen atom or a sulfur atom.).

TI Drug for treating migraine

REFERENCE COUNT: 29 THERE ARE 29 CITED REFERENCES AVAILABLE FOR THIS

RECORD. ALL CITATIONS AVAILABLE IN THE

RE FORMAT

IN Takeuchi, Megumi; Takayama, Makoto; Shirakura, Shiro; Kase, Hiroshi

AB Disclosed is a drug for treating migraine which contains, as an active constituent, a xanthine derivative represented by the formula (I) below or a pharmacol. acceptable salt thereof. (In the formulas, I; R1, R2 and R3 may be the same or different and resp. represent a hydrogen atom, a lower alkyl, a lower alkenyl or a lower alkynyl; R4 represents a cycloalkyl,  $-(CH_2)_n-R_5$  or one represented by the above formula (II); and X1 and X2 may be the same or different and resp. represent an oxygen atom or a sulfur atom.).

ST xanthine deriv analgesic migraine

IT Drug delivery systems

(capsules; xanthine derivs. for treating migraine)

IT Drug delivery systems

(injections; xanthine derivs. for treating migraine)

IT Headache

(migraine; xanthine derivs. for treating migraine)

IT Drug delivery systems

(tablets; xanthine derivs. for treating migraine)

IT Analgesics

Antimigraine agents

(xanthine derivs. for treating migraine)

IT 69-89-6D, Xanthine, derivs. and salts 31377-36-3 149744-74-1  
861387-30-6 861387-31-7

RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(xanthine derivs. for treating migraine)

L2 ANSWER 3 OF 13 CAPLUS COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 2005:547543 CAPLUS Full-text

DOCUMENT NUMBER: 143:53542

TITLE: Xanthine derivatives and salts and compositions for preventing and/or treating higher brain dysfunction

INVENTOR(S): Kase, Hiroshi; Nakagawa, Yutaka; Shiozaki, Shizuo; Kobayashi, Minoru; Toki, Shinichiro; Seno, Naoki; Ikeda, Ken

PATENT ASSIGNEE(S): Kyowa Hakko Kogyo Co., Ltd., Japan

SOURCE: PCT Int. Appl., 29 pp.  
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: Japanese

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005056016	A1	20050623	WO 2004-JP18765	
20041209				
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW			
RW:	BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, MR, NE, SN, TD, TG			
AU 2004296137	A1	20050623	AU 2004-296137	
20041209				
CA 2550130	A1	20050623	CA 2004-2550130	
20041209				
EP 1709966	A1	20061011	EP 2004-807124	
20041209				
R:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, IE, SI, LT, FI, RO, CY, TR, BG, CZ, EE, HU, PL, SK, IS			
CN 1889959	A	20070103	CN 2004-80036267	
20041209				
BR 2004017241	A	20070306	BR 2004-17241	
20041209				
US 20070078148	A1	20070405	US 2006-579829	
20060517				

MX 2006005965 A 20060809 MX 2006-5965  
20060525  
KR 2006124615 A 20061205 KR 2006-711123  
20060607  
IN 2006CN02490 A 20070608 IN 2006-CN2490  
20060706  
PRIORITY APPLN. INFO.: JP 2003-410432 A  
20031209 WO 2004-JP18765 W

20041209

OTHER SOURCE(S): MARPAT 143:53542

AB A preventive and/or therapeutic agent for higher brain dysfunctions which contains as an active ingredient a xanthine derivative represented, for example, by the following formula (I) or a pharmacol. acceptable salt thereof: (I) (II) wherein R1, R2, and R3 are the same or different and each represents hydrogen, lower alkyl, lower alkenyl, or lower alkynyl; R4 represents cycloalkyl, -(CH2)n-R5, or the formula (II) given above; and X1 and X2 are the same or different and each represents oxygen or sulfur. The higher brain dysfunction includes aging brain damage, brain trauma, cerebrovascular disease, memory disorder, thinking disorder, recognition disorder, behavior disorder, learning disorder, etc.

TI Xanthine derivatives and salts and compositions for preventing and/or treating higher brain dysfunction

REFERENCE COUNT: 32 THERE ARE 32 CITED REFERENCES AVAILABLE FOR THIS

RECORD. ALL CITATIONS AVAILABLE IN THE

RE FORMAT

TI Xanthine derivatives and salts and compositions for preventing and/or treating higher brain dysfunction

IN Kase, Hiroshi; Nakagawa, Yutaka; Shiozaki, Shizuo; Kobayashi, Minoru; Toki, Shinichiro; Seno, Naoki; Ikeda, Ken

L2 ANSWER 4 OF 13 CAPLUS COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 2005:99358 CAPLUS Full-text

DOCUMENT NUMBER: 142:162694

TITLE: Medicinal compositions containing adenosine A2A

receptor antagonists and other antidepressants

INVENTOR(S): Kase, Hiroshi; Kobayashi, Minoru; Shiozaki, Shizuo; Mori, Akihisa; Seno, Naoki

PATENT ASSIGNEE(S): Kyowa Hakko Kogyo Co., Ltd., Japan

SOURCE: PCT Int. Appl., 47 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: Japanese

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
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WO 2005009444	A1	20050203	WO 2004-JP10758	
20040722				

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ,

CA, CH,  
GB, GD,  
KZ, LC,  
NA, NI,  
SL, SY,  
ZM, ZW  
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM,  
ZW, AM,  
DE, DK,  
RO, SE,  
MR, NE,  
SN, TD, TG

CA 2533117 A1 20050203 CA 2004-2533117

20040722

EP 1655029 A1 20060510 EP 2004-748023

20040722

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE,  
MC, PT,

IE, SI, FI, RO, CY, TR, BG, CZ, EE, HU, PL, SK

US 20060241102 A1 20061026 US 2006-565239

20060119

NO 2006000958 A 20060425 NO 2006-958

20060227

PRIORITY APPLN. INFO.:

JP 2003-201549 A

20030725

WO 2004-JP10758 W

20040722

AB It is intended to provide medicinal compns. and the like useful in treating depression which contain a compound having an antagonism to adenosine A2A receptor (for example, (E)-8-(3,4-dimethoxystyryl)-1,3-diethyl-7-methyl-3,7-dihydro-1H-purin-2,6-dione) (I) or a pharmacol. acceptable salt thereof together with an antidepressant (for example, a tricyclic antidepressant, a tetracyclic antidepressant, a selective serotonin reuptake inhibitor, a selective noradrenaline reuptake inhibitor, a dopamine reuptake inhibitor, a serotonin/noradrenaline reuptake inhibitor, a monoamine oxidase inhibitor or a serotonin 2 antagonist). The effect of combination of I 0.08 and venlafaxine hydrochloride 5 mg/kg on depression in mice in forced swim test was examined

TI Medicinal compositions containing adenosine A2A receptor antagonists and

other antidepressants

REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS

RECORD. ALL CITATIONS AVAILABLE IN THE

RE FORMAT

IN Kase, Hiroshi; Kobayashi, Minoru; Shiozaki, Shizuo; Mori, Akihisa; Seno, Naoki

ST adenosine A2A receptor antagonist antidepressant combination;  
xanthine deriv antidepressant combination

L2 ANSWER 5 OF 13 CAPLUS COPYRIGHT 2009 ACS on STN  
ACCESSION NUMBER: 2004:1080800 CAPLUS Full-text  
DOCUMENT NUMBER: 142:33005  
TITLE: A method using an adenosine A2A receptor  
antagonist  
for treating an anxiety disorder  
INVENTOR(S): Kase, Hiroshi; Seno, Naoki; Shiozaki,  
Shizuo; Kobayashi, Minoru; Kase, Junya  
PATENT ASSIGNEE(S): Kyowa Hakko Kogyo Co., Ltd., Japan  
SOURCE: PCT Int. Appl., 96 pp.  
CODEN: PIXXD2  
DOCUMENT TYPE: Patent  
LANGUAGE: English  
FAMILY ACC. NUM. COUNT: 1  
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
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WO 2004108137	A1	20041216	WO 2004-JP8486	
20040610				
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ,				
CA, CH,				
CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI,				
GB, GD,				
GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR,				
KZ, LC,				
LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ,				
NA, NI,				
NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK,				
SL, SY,				
TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA,				
ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM,				
ZW, AM,				
AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ,				
DE, DK,				
EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT,				
RO, SE,				
SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML,				
MR, NE,				
SN, TD, TG				
AU 2004244906	A1	20041216	AU 2004-244906	
20040610				
CA 2528710	A1	20041216	CA 2004-2528710	
20040610				
EP 1631294	A1	20060308	EP 2004-746014	
20040610				
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE,				
MC, PT,				
IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU,				
PL, SK, HR				
CN 1787821	A	20060614	CN 2004-80012845	

20040610  
     BR 2004011120           A       20060718       BR 2004-11120  
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     JP 2006527264           T       20061130       JP 2006-516839  
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     US 20060281770          A1      20061214       US 2005-553250  
 20051017  
     KR 2006037252           A       20060503       KR 2005-721878  
 20051116  
     MX 2005013148           A       20060317       MX 2005-13148  
 20051205  
     NO 2005005907           A       20051213       NO 2005-5907  
 20051213  
     IN 2006CN00077          A       20070629       IN 2006-CN77  
 20060106  
 PRIORITY APPLN. INFO.:                   US 2003-509046P       P  
 20030610                                   US 2003-532793P       P  
 20031224                                   WO 2004-JP8486       W  
 20040610  
 OTHER SOURCE(S):           MARPAT 142:33005  
 AB    Anxiety disorders, such as panic disorder, agoraphobia, obsessive-  
       compulsive disorder, social phobia, post-traumatic stress  
       disorder, generalized anxiety disorder, specific phobia, or the  
       like, are treated by administering an effective amount of at least  
       one adenosine A2A receptor antagonist (e.g. a xanthine derivative)  
       to a patient in need thereof, optionally in combination with an  
       anxiolytic(s) other than the adenosine A2A receptor antagonist.  
 TI    A method using an adenosine A2A receptor antagonist for treating  
 an  
       anxiety disorder  
 REFERENCE COUNT:           5       THERE ARE 5 CITED REFERENCES AVAILABLE  
 FOR THIS  
                                  RECORD. ALL CITATIONS AVAILABLE IN THE  
 RE FORMAT  
 IN    Kase, Hiroshi; Seno, Naoki; Shiozaki, Shizuo; Kobayashi, Minoru;  
       Kase, Junya  
 AB    Anxiety disorders, such as panic disorder, agoraphobia, obsessive-  
       compulsive disorder, social phobia, post-traumatic stress  
       disorder, generalized anxiety disorder, specific phobia, or the  
       like, are treated by administering an effective amount of at least  
       one adenosine A2A receptor antagonist (e.g. a xanthine derivative)  
       to a patient in need thereof, optionally in combination with an  
       anxiolytic(s) other than the adenosine A2A receptor antagonist.  
 ST    adenosine A2A receptor antagonist anxiolytic; anxiety disorder  
 treatment  
       adenosine A2A receptor antagonist; xanthine deriv adenosine A2A  
       receptor antagonist anxiolytic  
 IT    69-89-6D, Xanthine, derivs.   51389-37-8   99331-25-6D,  
       Triazolopyrimidine, derivs.   155270-99-8   262452-04-0   377727-  
 87-2  
       RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL  
       (Biological study); USES (Uses)  
       (adenosine A2A receptor antagonist for treating anxiety  
 disorders)

<http://www.cas.org/support/stngen/stdoc/properties.html>

=> e 51-34-3/rn

E1	1	51-31-0/RN
E2	1	51-33-2/RN
E3	1 -->	51-34-3/RN
E4	1	51-35-4/RN
E5	1	51-36-5/RN
E6	1	51-37-6/RN
E7	1	51-38-7/RN
E8	1	51-39-8/RN
E9	1	51-40-1/RN
E10	1	51-41-2/RN
E11	1	51-42-3/RN
E12	1	51-43-4/RN

=> s e3

L3 1 51-34-3/RN

=> d 13

L3 ANSWER 1 OF 1 REGISTRY COPYRIGHT 2009 ACS on STN

RN 51-34-3 REGISTRY

ED Entered STN: 16 Nov 1984

CN Benzeneacetic acid,  $\alpha$ -(hydroxymethyl)-,  
(1 $\alpha$ , 2 $\beta$ , 4 $\beta$ , 5 $\alpha$ , 7 $\beta$ )-9-methyl-3-oxa-9-  
azatricyclo[3.3.1.0<sup>2,4</sup>]non-7-yl ester, ( $\alpha$ S)- (CA INDEX NAME)

OTHER CA INDEX NAMES:

CN 1 $\alpha$ H, 5 $\alpha$ H-Tropan-3 $\alpha$ -ol, 6 $\beta$ , 7 $\beta$ -epoxy-,  
(-)-tropate (ester) (8CI)

CN 3-Oxa-9-azatricyclo[3.3.1.0<sup>2,4</sup>]nonane, benzeneacetic acid deriv.

CN Benzeneacetic acid,  $\alpha$ -(hydroxymethyl)-,  
9-methyl-3-oxa-9-azatricyclo[3.3.1.0<sup>2,4</sup>]non-7-yl ester,  
[7(S)-(1 $\alpha$ , 2 $\beta$ , 4 $\beta$ , 5 $\alpha$ , 7 $\beta$ )]-

OTHER NAMES:

CN (-)-Hyoscine

CN (-)-Scopolamine

CN 6,7-Epoxytropine tropate

CN 6 $\beta$ , 7 $\beta$ -Epoxy-3 $\alpha$ -tropanyl S-(-)-tropate

CN 9-Methyl-3-oxa-9-azatricyclo[3.3.1.0<sup>2,4</sup>]nonan-7-ol (-)-tropate

CN Atrochin

CN Atroquin

CN Hyoscine

CN 1-Scopolamine

CN Scop

CN Scopine (-)-tropate

CN Scopine tropate

CN Scopoderm TTS

CN Scopolamine

CN SEE

CN Transcop

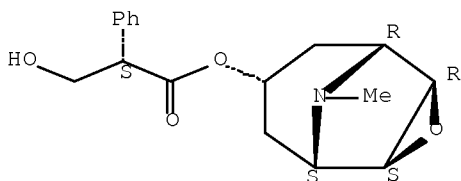
CN Transderm-Scop

CN Tropic acid ester with scopine

FS STEREOSEARCH

DR 58670-87-4, 14797-94-5, 97991-84-9, 65319-33-7, 28901-63-5,  
 226562-00-1  
 MF C17 H21 N O4  
 CI COM  
 LC STN Files: ADISNEWS, AGRICOLA, ANABSTR, BEILSTEIN\*, BIOSIS,  
 BIOTECHNO,  
 CA, CAPLUS, CASREACT, CBNB, CHEMCATS, CHEMLIST, CIN, CSCHEM,  
 DDFU,  
 DRUGU, EMBASE, GMELIN\*, HSDB\*, IFICDB, IFIPAT, IFIUDB,  
 IMSCOSEARCH,  
 IMSPRODUCT, IMSRESEARCH, IPA, MEDLINE, MRCK\*, MSDS-OHS,  
 NAPRALERT, PHAR,  
 PROMT, PS, RTECS\*, SPECINFO, TOXCENTER, USAN, USPAT2, USPATFULL,  
 USPATOLD, VETU  
 (\*File contains numerically searchable property data)  
 Other Sources: EINECS\*\*  
 (\*\*Enter CHEMLIST File for up-to-date regulatory information)

Absolute stereochemistry. Rotation (-).



\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

4918 REFERENCES IN FILE CA (1907 TO DATE)  
 32 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA  
 4923 REFERENCES IN FILE CAPLUS (1907 TO DATE)

=> e 69-89-6/rn

E1	1	69-81-8/RN
E2	1	69-86-3/RN
E3	1 -->	69-89-6/RN
E4	1	69-90-9/RN
E5	1	69-91-0/RN
E6	1	69-93-2/RN
E7	1	69-96-5/RN
E8	1	690-00-6/RN
E9	1	690-01-7/RN
E10	1	690-02-8/RN
E11	1	690-03-9/RN
E12	1	690-04-0/RN

=> s e3

L4 1 69-89-6/RN

=> d 14

L4 ANSWER 1 OF 1 REGISTRY COPYRIGHT 2009 ACS on STN  
 RN ~~69-89-6~~ REGISTRY  
 ED Entered STN: 16 Nov 1984  
 CN 1H-Purine-2,6-dione, 3,9-dihydro- (CA INDEX NAME)  
 OTHER CA INDEX NAMES:  
 CN 1H-Purine-2,6-dione, 3,7-dihydro- (9CI)  
 CN Xanthine (8CI)  
 OTHER NAMES:  
 CN 1H,3H,7H-Xanthine  
 CN 1H,3H,9H-Xanthine  
 CN 1H-Purine-2,6-diol  
 CN 2,6-Dioxo-1,2,3,6-tetrahydropurine  
 CN 2,6-Dioxopurine  
 CN 3,9-Dihydro-1H-purine-2,6-dione  
 CN 3,9-Dihydropurine-2,6-dione  
 CN 9H-Purine-2,6(1H,3H)-dione  
 CN Isoxanthine  
 CN NSC 14664  
 CN Pseudoxanthine  
 CN Purine-2,6(1H,3H)-dione  
 CN Xan  
 CN Xanthic oxide  
 CN Xanthin  
 DR 16819-86-6, 51953-26-5, 6050-36-8, 6053-41-4, 28522-58-9, 33669-  
 67-9,  
 42911-15-9  
 MF C5 H4 N4 O2  
 CI COM  
 LC STN Files: ADISNEWS, AGRICOLA, ANABSTR, BEILSTEIN\*, BIOSIS,  
 BIOTECHNO,  
 CA, CABA, CAPLUS, CASREACT, CBNB, CHEMCATS, CHEMINFORMRX,  
 CHEMLIST, CIN,  
 CSCHEM, DDFU, DETHERM\*, DRUGU, EMBASE, GMELIN\*, IFICDB, IFIPAT,  
 IFIUDB,  
 IPA, MEDLINE, MRCK\*, MSDS-OHS, NAPRALERT, PIRA, PROMT, RTECS\*,  
 SPECINFO,  
 TOXCENTER, USPAT2, USPATFULL, USPATOLD  
 (\*File contains numerically searchable property data)  
 Other Sources: DSL\*\*, EINECS\*\*, TSCA\*\*  
 (\*\*Enter CHEMLIST File for up-to-date regulatory information)



\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

5562 REFERENCES IN FILE CA (1907 TO DATE)  
 926 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA  
 5580 REFERENCES IN FILE CAPLUS (1907 TO DATE)

=> e 51389-37-8/rn

E1	1	51389-35-6/RN
E2	1	51389-36-7/RN
E3	1 -->	51389-37-8/RN
E4	1	51389-38-9/RN
E5	1	51389-39-0/RN
E6	1	51389-40-3/RN
E7	1	51389-41-4/RN
E8	1	51389-42-5/RN
E9	1	51389-43-6/RN
E10	1	51389-44-7/RN
E11	1	51389-45-8/RN
E12	1	51389-46-9/RN

=> s e3

L5 1 51389-37-8/RN

=> d 15

L5 ANSWER 1 OF 1 REGISTRY COPYRIGHT 2009 ACS on STN

RN ~~51389-37-8~~ REGISTRY

ED Entered STN: 16 Nov 1984

CN 1H-Purine-2,6-dione, 3,7-dihydro-1,3,7-trimethyl-8-[(1E)-2-(3,4,5-trimethoxyphenyl)ethenyl]- (CA INDEX NAME)

OTHER CA INDEX NAMES:

CN 1H-Purine-2,6-dione, 3,7-dihydro-1,3,7-trimethyl-8-[2-(3,4,5-trimethoxyphenyl)ethenyl]-, (E)-

OTHER NAMES:

CN KF 18446

CN trans-8-(3,4,5-Trimethoxystyryl)caffeine

FS STEREOSEARCH

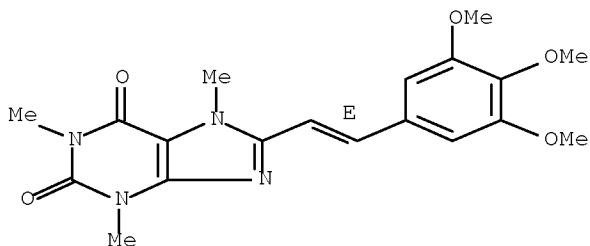
MF C19 H22 N4 O5

LC STN Files: BEILSTEIN\*, BIOSIS, CA, CAPLUS, RTECS\*, TOXCENTER, USPAT2,

USPATFULL

(\*File contains numerically searchable property data)

Double bond geometry as shown.



\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

14 REFERENCES IN FILE CA (1907 TO DATE)  
14 REFERENCES IN FILE CAPLUS (1907 TO DATE)

=> e 141807-96-7/rn

E1	1	141807-94-5/RN
E2	1	141807-95-6/RN
E3	1 -->	141807-96-7/RN
E4	1	141807-97-8/RN
E5	1	141807-98-9/RN
E6	1	141807-99-0/RN
E7	1	141808-00-6/RN
E8	1	141808-01-7/RN
E9	1	141808-02-8/RN
E10	1	141808-03-9/RN
E11	1	141808-04-0/RN
E12	1	141808-05-1/RN

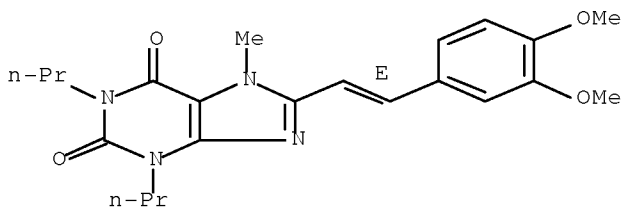
=> s e3

L6 1 141807-96-7/RN

=> d 16

L6 ANSWER 1 OF 1 REGISTRY COPYRIGHT 2009 ACS on STN  
RN 141807-96-7 REGISTRY  
ED Entered STN: 12 Jun 1992  
CN 1H-Purine-2,6-dione, 8-[(1E)-2-(3,4-dimethoxyphenyl)ethenyl]-3,7-dihydro-7-methyl-1,3-dipropyl- (CA INDEX NAME)  
OTHER CA INDEX NAMES:  
CN 1H-Purine-2,6-dione, 8-[2-(3,4-dimethoxyphenyl)ethenyl]-3,7-dihydro-7-methyl-1,3-dipropyl-, (E)-  
OTHER NAMES:  
CN KF 17837  
CN KW 17837  
FS STEREOSEARCH  
MF C22 H28 N4 O4  
SR CA  
LC STN Files: ADISINSIGHT, BEILSTEIN\*, BIOSIS, BIOTECHNO, CA, CAPLUS, EMBASE, IMSDRUGNEWS, IMSRESEARCH, PROUSDDR, RTECS\*, TOXCENTER, USPAT2, USPATFULL  
(\*File contains numerically searchable property data)

Double bond geometry as shown.



\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

55 REFERENCES IN FILE CA (1907 TO DATE)

55 REFERENCES IN FILE CAPLUS (1907 TO DATE)

=> e 155270-99-8/rn

E1	1	155270-97-6/RN
E2	1	155270-98-7/RN
E3	1 -->	155270-99-8/RN
E4	1	155271-00-4/RN
E5	1	155271-01-5/RN
E6	1	155271-02-6/RN
E7	1	155271-03-7/RN
E8	1	155271-04-8/RN
E9	1	155271-05-9/RN
E10	1	155271-06-0/RN
E11	1	155271-07-1/RN
E12	1	155271-08-2/RN

=> s e3

L7 1 155270-99-8/RN

=> d 17

L7 ANSWER 1 OF 1 REGISTRY COPYRIGHT 2009 ACS on STN

RN 155270-99-8 REGISTRY

ED Entered STN: 24 May 1994

CN 1H-Purine-2,6-dione, 8-[(1E)-2-(3,4-dimethoxyphenyl)ethenyl]-1,3-diethyl-

3,7-dihydro-7-methyl- (CA INDEX NAME)

OTHER CA INDEX NAMES:

CN 1H-Purine-2,6-dione, 8-[2-(3,4-dimethoxyphenyl)ethenyl]-1,3-diethyl-3,7-

dihydro-7-methyl-, (E)-

OTHER NAMES:

CN Istradefylline

CN KW 6002

FS STEREOSEARCH

MF C20 H24 N4 O4

CI COM

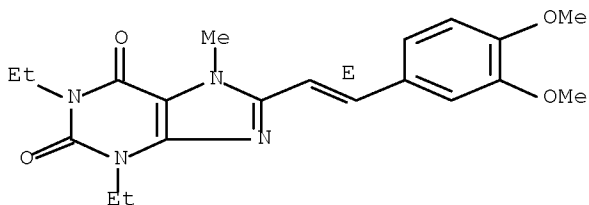
SR CA

LC STN Files: ADISINSIGHT, ADISNEWS, AGRICOLA, BIOSIS, BIOTECHNO, CA,

CAPLUS, CASREACT, CBNB, CHEMCATS, CIN, EMBASE, IMSPATENTS,

IMSRESEARCH,  
 IPA, MEDLINE, PHAR, PROMT, PROUSDDR, RTECS\*, SYNTHLINE,  
 TOXCENTER, USAN,  
 USPAT2, USPATFULL  
 (\*File contains numerically searchable property data)

Double bond geometry as shown.



\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

103 REFERENCES IN FILE CA (1907 TO DATE)  
 104 REFERENCES IN FILE CAPLUS (1907 TO DATE)

=> e 155272-00-7/rn

E1	1	155271-98-0/RN
E2	1	155271-99-1/RN
E3	1	--> 155272-00-7/RN
E4	1	155272-01-8/RN
E5	1	155272-02-9/RN
E6	1	155272-03-0/RN
E7	1	155272-04-1/RN
E8	1	155272-05-2/RN
E9	1	155272-06-3/RN
E10	1	155272-07-4/RN
E11	1	155272-08-5/RN
E12	1	155272-09-6/RN

=> s e3

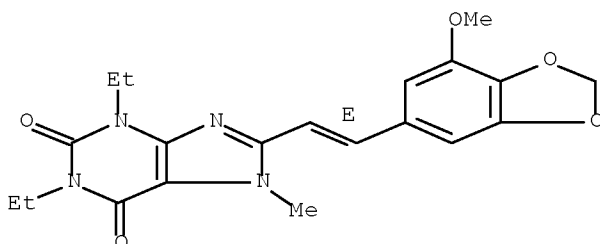
L8 1 155272-00-7/RN

=> d 18

L8 ANSWER 1 OF 1 REGISTRY COPYRIGHT 2009 ACS on STN  
 RN 155272-00-7 REGISTRY  
 ED Entered STN: 24 May 1994  
 CN 1H-Purine-2,6-dione, 1,3-diethyl-3,7-dihydro-8-[(1E)-2-(7-methoxy-1,3-benzodioxol-5-yl)ethenyl]-7-methyl- (CA INDEX NAME)  
 OTHER CA INDEX NAMES:  
 CN 1H-Purine-2,6-dione, 1,3-diethyl-3,7-dihydro-8-[2-(7-methoxy-1,3-benzodioxol-5-yl)ethenyl]-7-methyl-, (E)-  
 OTHER NAMES:

CN (E)-1,3-Diethyl-8-(3,4-methylenedioxy-5-methoxystyryl)-7-methylxanthine  
 FS STEREOSEARCH  
 MF C20 H22 N4 O5  
 SR CA  
 LC STN Files: CA, CAPLUS, RTECS\*, TOXCENTER, USPAT2, USPATFULL  
 (\*File contains numerically searchable property data)

Double bond geometry as shown.



\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

8 REFERENCES IN FILE CA (1907 TO DATE)  
 8 REFERENCES IN FILE CAPLUS (1907 TO DATE)

=> e 1H-Purine-2,6-dione, 8-[(1E)-2-(3,4-dimethoxyphenyl)ethenyl]-1,3-diethyl-3,7-dihydro-7-methyl-/cn

E1 1 1H-PURINE-2,6-DIONE, 8,9-DIHYDRO-8-THIOXO-/CN  
 E2 1 1H-PURINE-2,6-DIONE, 8,9-DIHYDRO-9-METHYL-8-(1,2,6,9-TETRAHYDRO-9-METHYL-2,6-DIOXO-8H-PURIN-8-YLIDENE)-/CN  
 E3 0 --> 1H-PURINE-2,6-DIONE, 8-(1E)-2-(3,4-DIMETHOXYPHENYL)ETHENYL  
 -1,3-DIETHYL-3,7-DIHYDRO-7-METHYL-/CN  
 E4 1 1H-PURINE-2,6-DIONE, 8-(((2-CHLOROPHENYL)METHYL)AMINO)METHYL-3,7-DIHYDRO-1,3-DIMETHYL-/CN  
 E5 1 1H-PURINE-2,6-DIONE, 8-(((2-CHLOROPHENYL)METHYL)AMINO)METHYL-3,9-DIHYDRO-1,3-DIMETHYL-/CN  
 E6 1 1H-PURINE-2,6-DIONE, 8-(((1,1-DIMETHYLETHYL)AMINO)METHYL)-3,7-DIHYDRO-1,3,7-TRIMETHYL-/CN  
 E7 1 1H-PURINE-2,6-DIONE, 8-(((1,1-DIMETHYLETHYL)THIO)METHYL)-3,9-DIHYDRO-1,3-DIMETHYL-/CN  
 E8 1 1H-PURINE-2,6-DIONE, 8-(((1,2-DIHYDRO-2-OXO-4-QUINOLINYL)METHYL)THIO)-3,7-DIHYDRO-1,3,7-TRIMETHYL-/CN  
 E9 1 1H-PURINE-2,6-DIONE, 8-(((1,2-DIHYDRO-2-OXO-4-QUINOLINYL)METHYL)THIO)-3,7-DIHYDRO-1,3-DIMETHYL-7-(4-METHYLPHENYL)METHYL

```

) - /CN
E10      1      1H-PURINE-2,6-DIONE, 8-(((1,2-DIHYDRO-2-OXO-4-
QUINOLINYL)MET
HYL)THIO)-3,7-DIHYDRO-1,3-DIMETHYL-7-(1-
METHYLETHYL)-/CN
E11      1      1H-PURINE-2,6-DIONE, 8-(((1,2-DIHYDRO-2-OXO-4-
QUINOLINYL)MET
HYL)THIO)-3,7-DIHYDRO-1,3-DIMETHYL-7-(1-
NAPHTHALENYLMETHYL)-
/CN
E12      1      1H-PURINE-2,6-DIONE, 8-(((1,2-DIHYDRO-2-OXO-4-
QUINOLINYL)MET
HYL)THIO)-3,7-DIHYDRO-1,3-DIMETHYL-7-(PHENYLMETHYL)-
/CN

=> set expand continuous
SET COMMAND COMPLETED

=> e 1H-Purine-2,6-dione, 8-[2-(3,4-dimethoxyphenyl)ethenyl]-1,3-
diethyl-3,7- dihydro-7-methyl-, (E)-/cn
E13      1      1H-PURINE-2,6-DIONE, 8,9-DIHYDRO-8-THIOXO-/CN
E14      1      1H-PURINE-2,6-DIONE, 8,9-DIHYDRO-9-METHYL-8-
(1,2,6,9-TETRAHY
DRO-9-METHYL-2,6-DIOXO-8H-PURIN-8-YLIDENE)-/CN
E15      0 --> 1H-PURINE-2,6-DIONE, 8-2-(3,4-
DIMETHOXYPHENYL)ETHENYL -1,3-
DIETHYL-3,7- DIHYDRO-7-METHYL-, (E)-/CN
E16      1      1H-PURINE-2,6-DIONE, 8-(((2-
CHLOROPHENYL)METHYL)AMINO)METHY
L)-3,7-DIHYDRO-1,3-DIMETHYL-/CN
E17      1      1H-PURINE-2,6-DIONE, 8-(((2-
CHLOROPHENYL)METHYL)AMINO)METHY
L)-3,9-DIHYDRO-1,3-DIMETHYL-/CN
E18      1      1H-PURINE-2,6-DIONE, 8-(((1,1-
DIMETHYLETHYL)AMINO)METHYL)-3,
7-DIHYDRO-1,3,7-TRIMETHYL-/CN
E19      1      1H-PURINE-2,6-DIONE, 8-(((1,1-
DIMETHYLETHYL)THIO)METHYL)-3,9
-DIHYDRO-1,3-DIMETHYL-/CN
E20      1      1H-PURINE-2,6-DIONE, 8-(((1,2-DIHYDRO-2-OXO-4-
QUINOLINYL)MET
HYL)THIO)-3,7-DIHYDRO-1,3,7-TRIMETHYL-/CN
E21      1      1H-PURINE-2,6-DIONE, 8-(((1,2-DIHYDRO-2-OXO-4-
QUINOLINYL)MET
HYL)THIO)-3,7-DIHYDRO-1,3-DIMETHYL-7-(4-
METHYLPHENYL)METHYL
)-/CN
E22      1      1H-PURINE-2,6-DIONE, 8-(((1,2-DIHYDRO-2-OXO-4-
QUINOLINYL)MET
HYL)THIO)-3,7-DIHYDRO-1,3-DIMETHYL-7-(1-
METHYLETHYL)-/CN
E23      1      1H-PURINE-2,6-DIONE, 8-(((1,2-DIHYDRO-2-OXO-4-
QUINOLINYL)MET
HYL)THIO)-3,7-DIHYDRO-1,3-DIMETHYL-7-(1-
NAPHTHALENYLMETHYL)-
/CN
E24      1      1H-PURINE-2,6-DIONE, 8-(((1,2-DIHYDRO-2-OXO-4-

```

QUINOLINYL)MET

HYL) THIO)-3,7-DIHYDRO-1,3-DIMETHYL-7-(PHENYLMETHYL)-  
/CN

=> e Istradefylline/cn

E25	1	ISTONIL/CN
E26	1	ISTOPIRIN/CN
E27	1 -->	ISTRADEFYLLINE/CN
E28	1	ISTROEKOL/CN
E29	1	ISTRONA/CN
E30	1	ISU-CCUR/CN
E31	1	ISUBGOL/CN
E32	1	ISUHUMAN/CN
E33	1	ISUMELINE/CN
E34	1	ISUPREL/CN
E35	1	ISUPREN/CN
E36	1	ISURETIN/CN

=> e KW 6002/cn

E37	1	KW 6/CN
E38	2	KW 600/CN
E39	1 -->	KW 6002/CN
E40	1	KW 600S/CN
E41	1	KW 6055/CN
E42	1	KW 6066N/CN
E43	1	KW 6151/CN
E44	1	KW 622/CN
E45	1	KW 6629/CN
E46	1	KW 677/CN
E47	1	KW 678/CN
E48	1	KW 7/CN

=> s e27

L9 1 ISTRADefYLLINE/CN

=> d 19

L9 ANSWER 1 OF 1 REGISTRY COPYRIGHT 2009 ACS on STN

RN 155270-99-8 REGISTRY

ED Entered STN: 24 May 1994

CN 1H-Purine-2,6-dione, 8-[(1E)-2-(3,4-dimethoxyphenyl)ethenyl]-1,3-diethyl-

3,7-dihydro-7-methyl- (CA INDEX NAME)

OTHER CA INDEX NAMES:

CN 1H-Purine-2,6-dione, 8-[2-(3,4-dimethoxyphenyl)ethenyl]-1,3-diethyl-3,7-

dihydro-7-methyl-, (E)-

OTHER NAMES:

CN Istradefylline

CN KW 6002

FS STEREOSEARCH

MF C20 H24 N4 O4

CI COM

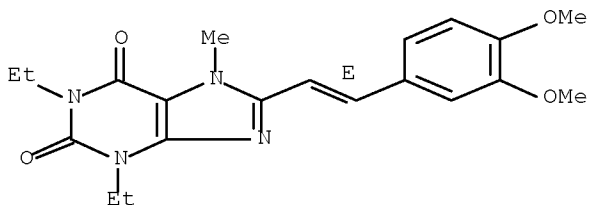
SR CA

LC STN Files: ADISINSIGHT, ADISNEWS, AGRICOLA, BIOSIS, BIOTECHNO, CA,

CAPLUS, CASREACT, CBNB, CHEMCATS, CIN, EMBASE, IMSPATENTS,

IMSRESEARCH,  
 IPA, MEDLINE, PHAR, PROMT, PROUSDDR, RTECS\*, SYNTHLINE,  
 TOXCENTER, USAN,  
 USPAT2, USPATFULL  
 (\*File contains numerically searchable property data)

Double bond geometry as shown.



\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

103 REFERENCES IN FILE CA (1907 TO DATE)  
 104 REFERENCES IN FILE CAPLUS (1907 TO DATE)

=> s e39

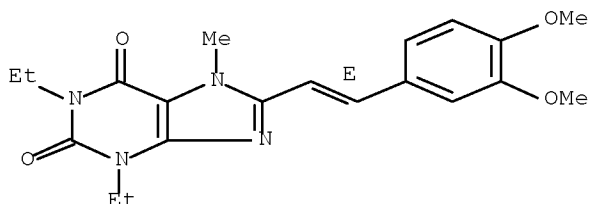
L10 1 "KW 6002"/CN

=> d l10

L10 ANSWER 1 OF 1 REGISTRY COPYRIGHT 2009 ACS on STN  
 RN 155270-99-8 REGISTRY  
 ED Entered STN: 24 May 1994  
 CN 1H-Purine-2,6-dione, 8-[(1E)-2-(3,4-dimethoxyphenyl)ethenyl]-1,3-diethyl-  
 3,7-dihydro-7-methyl- (CA INDEX NAME)  
 OTHER CA INDEX NAMES:  
 CN 1H-Purine-2,6-dione, 8-[2-(3,4-dimethoxyphenyl)ethenyl]-1,3-diethyl-3,7-  
 dihydro-7-methyl-, (E)-  
 OTHER NAMES:  
 CN Istradefylline  
 CN KW 6002  
 FS STEREOSEARCH  
 MF C20 H24 N4 O4  
 CI COM  
 SR CA  
 LC STN Files: ADISINSIGHT, ADISNEWS, AGRICOLA, BIOSIS, BIOTECHNO,  
 CA,  
 CAPLUS, CASREACT, CBNB, CHEMCATS, CIN, EMBASE, IMSPATENTS,  
 IMSRESEARCH,  
 IPA, MEDLINE, PHAR, PROMT, PROUSDDR, RTECS\*, SYNTHLINE,  
 TOXCENTER, USAN,  
 USPAT2, USPATFULL

(\*File contains numerically searchable property data)

Double bond geometry as shown.



\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

103 REFERENCES IN FILE CA (1907 TO DATE)

104 REFERENCES IN FILE CAPLUS (1907 TO DATE)

<http://www.cas.org/legal/infopolicy.html>

This file contains CAS Registry Numbers for easy and accurate substance identification.

=> s 17 or 19 or 110

104 L7

104 L9

104 L10

L11 104 L7 OR L9 OR L10

=> s 111 and brain, disease/it

495101 BRAIN/IT

2040 BRAINS/IT

495220 BRAIN/IT

((BRAIN OR BRAINS)/IT)

867672 DISEASE/IT

105349 DISEASES/IT

913630 DISEASE/IT

((DISEASE OR DISEASES)/IT)

71978 BRAIN, DISEASE/IT

((BRAIN(W)DISEASE)/IT)

L12 6 L11 AND BRAIN, DISEASE/IT

=> s (17 or 19 or 110)

104 L7

104 L9

104 L10

L13 104 (L7 OR L9 OR L10)

=> s 113 and learning disorders/it

18467 LEARNING/IT

4 LEARNINGS/IT

18470 LEARNING/IT

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                ((LEARNING OR LEARNINGS)/IT)
145760 DISORDERS/IT
        1263 LEARNING DISORDERS/IT
                ((LEARNING(W)DISORDERS)/IT)
L14          1 L13 AND LEARNING DISORDERS/IT

=> s l13 and memory disorders/it
        104513 MEMORY/IT
        1779 MEMORIES/IT
        104686 MEMORY/IT
                ((MEMORY OR MEMORIES)/IT)
        145760 DISORDERS/IT
        2980 MEMORY DISORDERS/IT
                ((MEMORY(W)DISORDERS)/IT)
L15          1 L13 AND MEMORY DISORDERS/IT

=> s l13 and mental and behavioral disorders/it
        66412 MENTAL
        5 MENTALS
        66416 MENTAL
                (MENTAL OR MENTALS)
        31717 BEHAVIORAL/IT
        31717 BEHAVIORAL/IT
                ((BEHAVIORAL OR BEHAVIOURAL)/IT)
        145760 DISORDERS/IT
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L17  ANSWER 1 OF 2  CAPLUS  COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER:      2004:566535  CAPLUS  Full-text
DOCUMENT NUMBER:      141:99728
TITLE:                  A method using
                        (E)-8-(3,4-dimethoxystyryl)-1,3-diethyl-7-
                        methylxanthine for treating behavioral
disorders
INVENTOR(S):           Shiozaki, Shizuo; Shimada, Junichi; Kase,
Hiroshi;
                        Shindo, Mayumi
PATENT ASSIGNEE(S):    Kyowa Hakko Kogyo Co., Ltd., Japan
SOURCE:                PCT Int. Appl., 24 pp.
                        CODEN: PIXXD2
DOCUMENT TYPE:          Patent

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LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004058139	A2	20040715	WO 2003-IB6455	
20031224 <--				
WO 2004058139	A3	20041104		
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RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
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20031224 <--				
AU 2003299432	A1	20040722	AU 2003-299432	
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EP 1581163	A2	20051005	EP 2003-799729	
20031224 <--				
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
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US 20090023755	A1	20090122	US 2008-239955	
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PRIORITY APPLN. INFO.:			US 2002-509039P	P
20021227 <--				
20031224			WO 2003-IB6455	W
			US 2005-539574	A1

20050728

AB The invention provides a method of treating behavioral disorders such as attention deficit hyperactivity disorder, comprising administering an effective amount of (E)-8-(3,4-dimethoxystyryl)-1,3-diethyl-7-methylxanthine or a pharmaceutically acceptable salt to a patient. This method may also be used for Tic/Tourette's disorder.

TI A method using (E)-8-(3,4-dimethoxystyryl)-1,3-diethyl-7-methylxanthine for treating behavioral disorders

REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS

RECORD. ALL CITATIONS AVAILABLE IN THE

RE FORMAT

PRAI US 2002-509039P	P	20021227	<--
WO 2003-IB6455	W	20031224	
US 2005-539574	A1	20050728	

IT Brain, disease

(Gilles de la Tourette syndrome, tic/Tourette's disorder;

xanthine

derivative for treatment of behavioral disorders)

IT 155270-99-8

RL: PAC (Pharmacological activity); PRP (Properties); THU (Therapeutic

use); BIOL (Biological study); USES (Uses)

(xanthine derivative for treatment of behavioral disorders)

L17 ANSWER 2 OF 2 CAPLUS COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 1998:644563 CAPLUS [Full-text](#)

DOCUMENT NUMBER: 130:33316

TITLE: Adenosine A2A receptors modify motor function in

MPTP-treated common marmosets

AUTHOR(S): Kanda, Tomoyuki; Tashiro, Tomomi; Kuwana, Yoshihisa;

Jenner, Peter

CORPORATE SOURCE: Pharmaceutical Research Institute, Kyowa Hakko Kogyo

Co Ltd, Shizuoka, 411-8731, Japan

SOURCE: NeuroReport (1998), 9(12), 2857-2860

CODEN: NERPEZ; ISSN: 0959-4965

PUBLISHER: Lippincott Williams & Wilkins

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Both adenosine A1 and A2 receptor populations are located in the striatum and can modify locomotor activity, and they may form a therapeutic target for Parkinson's disease (PD). Administration of the selective adenosine A2A antagonist (E)-1,3-diethyl-8-(3,4-dimethoxystyryl)-7-methyl-3,7-dihydro-1H-purine-2,6-dione (KW-6002) to MPTP-treated common marmosets increased locomotor activity. In contrast, administration of the selective A1 receptor antagonist 1,3-dipropyl-8-cyclopentylxanthine (DPCPX) had no effect on locomotion. Administration of the adenosine A2A receptor agonist 2-[p-[2-(2-aminoethylamino) carbonyl ethyl] phenethyl amino]-5'-N-ethylcarboxamidoadenosine (APEC) dose dependently suppressed basal locomotor activity. A minimally ED of APEC (0.62 mg/kg, i.p) completely reversed the increase in

locomotor activity produced by administration of KW-6002. The adenosine A2A receptor appears to be an important target for the treatment of basal ganglia disorders, particularly PD.

TI Adenosine A2A receptors modify motor function in MPTP-treated common marmosets

REFERENCE COUNT: 18 THERE ARE 18 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

SO NeuroReport (1998), 9(12), 2857-2860  
CODEN: NERPEZ; ISSN: 0959-4965

IT Brain, disease  
(basal ganglion; adenosine A2A receptors modify motor function in MPTP-treated common marmoset Parkinsonism model)

IT 155270-99-8  
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(adenosine A2A receptors modify motor function in MPTP-treated common marmoset Parkinsonism model)

=> d 118 ibib abs ti hit 1-2

L18 ANSWER 1 OF 2 CAPLUS COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 2006:463565 CAPLUS Full-text

DOCUMENT NUMBER: 144:460860

TITLE: Adenosine A2a receptor antagonists for the treatment of extrapyramidal syndrome and other movement disorders

INVENTOR(S): Grzelak, Michael; Hunter, John; Pond, Annamarie; Varty, Geoffrey

PATENT ASSIGNEE(S): USA

SOURCE: U.S. Pat. Appl. Publ., 27 pp., Cont.-in-part of U.S. Ser. No. 738,906.

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 3

PATENT INFORMATION: CODEN: USXXCO

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US 20060106040	A1	20060518	US 2005-234644	
20050923 <--				
US 20040138235	A1	20040715	US 2003-738906	
20031217 <--				
US 7414058	B2	20080819		

CA 2510655	A1	20050519	CA 2003-2510655
20031217 <--			
AU 2003304527	A1	20050526	AU 2003-304527
20031217 <--			
EP 1578409	A1	20050928	EP 2003-818838
20031217 <--			
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BR 2003017436	A	20051116	BR 2003-17436
20031217 <--			
JP 2006514697	T	20060511	JP 2005-510511
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NZ 540493	A	20080430	NZ 2003-540493
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CN 101310724	A	20081126	CN 2008-10136154
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US 20060128694	A1	20060615	US 2005-249796
20051013 <--			
AU 2006294919	A1	20070405	AU 2006-294919
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CA 2623040	A1	20070405	CA 2006-2623040
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WO 2007038212	A1	20070405	WO 2006-US36864
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GB, GD,			
GE, GH, GM, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM,			
KN, KP,			
KR, KZ, LA, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG,			
MK, MN,			
MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT,			
RO, RS,			
RU, SC, SD, SE, SG, SK, SL, SM, SV, SY, TJ, TM, TN, TR,			
TT, TZ,			
UA, UG, US, UZ, VC, VN, ZA, ZM, ZW			
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR,			
HU, IE,			
IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR,			
BF, BJ,			
CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG,			
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EP 1940408	A1	20080709	EP 2006-815125
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JP 2009508967	T	20090305	JP 2008-532393

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     MX 2008004006           A       20080410       MX 2008-4006  
 20080324  
     CN 101312731           A       20081126       CN 2006-80043146  
 20080519  
 PRIORITY APPLN. INFO.:                   US 2002-435321P       P  
 20021219 <--                           US 2003-738906       A2  
  
 20031217                               CN 2003-80107087       A3  
  
 20031217                               WO 2003-US40456       W  
  
 20031217                               US 2005-234644       A2  
  
 20050923                               WO 2006-US36864       W  
  
 20060921  
 OTHER SOURCE(S):           MARPAT 144:460860  
 AB    The invention discloses a method for the treatment or prevention  
       of extrapyramidal syndrome (EPS), dystonia, restless legs syndrome  
       (RLS) or periodic leg movement in sleep (PLMS), comprising the  
       administration of an adenosine A2a receptor antagonist, alone or  
       in combination with other agents useful for treating EPS,  
       dystonia, RLS or PLMS.  
 TI    Adenosine A2a receptor antagonists for the treatment of  
 extrapyramidal  
       syndrome and other movement disorders  
 PRAI US 2002-435321P       P       20021219 <--  
       US 2003-738906       A2       20031217  
       CN 2003-80107087       A3       20031217  
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       US 2005-234644       A2       20050923  
       WO 2006-US36864       W       20060921  
 IT    Mental and behavioral disorders  
       (depression, dystonia from antidepressant use; adenosine A2a  
 receptor  
       antagonists for treatment of extrapyramidal syndrome and other  
 movement  
       disorders)  
 IT    Mental and behavioral disorders  
       (psychosis, extrapyramidal syndrome from typical or atypical  
       antipsychotic use; adenosine A2a receptor antagonists for  
 treatment of  
       extrapyramidal syndrome and other movement disorders)  
 IT    59-92-7, Levodopa, biological studies 322-35-0, Benserazide  
       7439-89-6D, Iron, salts 12794-10-4D, Benzodiazepine, derivs.  
       28860-95-9, Carbidopa 155270-99-8 377727-26-9  
       RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL  
       (Biological study); USES (Uses)  
       (adenosine A2a receptor antagonists for treatment of  
 extrapyramidal  
       syndrome and other movement disorders)  
  
 L18 ANSWER 2 OF 2 CAPLUS COPYRIGHT 2009 ACS on STN  
 ACCESSION NUMBER:       2004:566535 CAPLUS Full-text  
 DOCUMENT NUMBER:       141:99728  
 TITLE:                 A method using

(E)-8-(3,4-dimethoxystyryl)-1,3-diethyl-7-methylxanthine for treating behavioral

disorders

INVENTOR(S):

Hiroshi;

Shiozaki, Shizuo; Shimada, Junichi; Kase,

Shindo, Mayumi

PATENT ASSIGNEE(S):

Kyowa Hakko Kogyo Co., Ltd., Japan

SOURCE:

PCT Int. Appl., 24 pp.

CODEN: PIXXD2

DOCUMENT TYPE:

Patent

LANGUAGE:

English

FAMILY ACC. NUM. COUNT:

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PATENT INFORMATION:

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GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR,				
KZ, LC,				
LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ,				
NI, NO,				
NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL,				
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   WO 2003-IB6455       W  
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 20050728  
 AB    The invention provides a method of treating behavioral disorders  
       such as attention deficit hyperactivity disorder, comprising  
       administering an effective amount of (E)-8-(3,4-dimethoxystyryl)-  
       1,3-diethyl-7-methylxanthine or a pharmaceutically acceptable salt  
       to a patient. This method may also be used for Tic/Tourette's  
       disorder.  
 TI    A method using (E)-8-(3,4-dimethoxystyryl)-1,3-diethyl-7-  
 methylxanthine  
       for treating behavioral disorders  
 REFERENCE COUNT:           2       THERE ARE 2 CITED REFERENCES AVAILABLE  
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 PRAI US 2002-509039P       P       20021227 <--  
       WO 2003-IB6455       W       20031224  
       US 2005-539574       A1       20050728  
 IT    Brain, disease  
       (Gilles de la Tourette syndrome, tic/Tourette's disorder;  
 xanthine  
       derivative for treatment of behavioral disorders)  
 IT    Mental and behavioral disorders  
       (attention deficit hyperactivity disorder; xanthine derivative  
 for  
       treatment of behavioral disorders)  
 IT    Drug delivery systems  
       (capsules; xanthine derivative for treatment of behavioral  
       disorders)  
 IT    Drug delivery systems  
       (injections; xanthine derivative for treatment of behavioral  
       disorders)  
 IT    Behavior  
       (locomotor; xanthine derivative for treatment of behavioral  
       disorders)  
 IT    Drug delivery systems  
       (tablets; xanthine derivative for treatment of behavioral  
       disorders)  
 IT    Central nervous system  
       (tic/Tourette's disorder; xanthine derivative for treatment of  
       behavioral disorders)  
 IT    Mental and behavioral disorders  
       (xanthine derivative for treatment of behavioral  
       disorders)  
 IT    155270-99-8  
       RL: PAC (Pharmacological activity); PRP (Properties); THU  
       (Therapeutic  
       use); BIOL (Biological study); USES (Uses)

(xanthine derivative for treatment of behavioral disorders)

<http://www.cas.org/support/stngen/stndoc/properties.html>

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E4	1	155271-00-4/RN
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E6	1	155271-02-6/RN
E7	1	155271-03-7/RN
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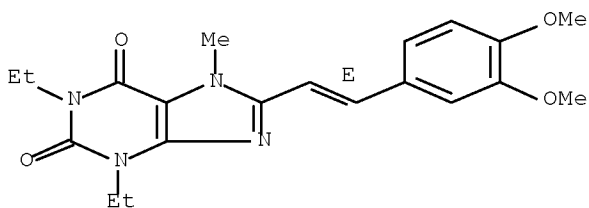
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L1 ANSWER 1 OF 1 REGISTRY COPYRIGHT 2009 ACS on STN  
RN 155270-99-8 REGISTRY  
ED Entered STN: 24 May 1994  
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3,7-dihydro-7-methyl- (CA INDEX NAME)  
OTHER CA INDEX NAMES:  
CN 1H-Purine-2,6-dione, 8-[2-(3,4-dimethoxyphenyl)ethenyl]-1,3-diethyl-3,7-  
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OTHER NAMES:  
CN Istradefylline  
CN KW 6002  
FS STEREOSEARCH  
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CAPLUS, CASREACT, CBNB, CHEMCATS, CIN, EMBASE, IMSPATENTS, IMSRESEARCH,  
IPA, MEDLINE, PHAR, PROMT, PROUSDDR, RTECS\*, SYNTHLINE, TOXCENTER, USAN,  
USPAT2, USPATFULL  
(\*File contains numerically searchable property data)

Double bond geometry as shown.



\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

103 REFERENCES IN FILE CA (1907 TO DATE)

104 REFERENCES IN FILE CAPLUS (1907 TO DATE)

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E14	1	ISTOPIRIN/CN
E15	1 -->	ISTRADEFYLLINE/CN
E16	1	ISTROEKOL/CN
E17	1	ISTRONA/CN
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E21	1	ISUMELINE/CN
E22	1	ISUPREL/CN
E23	1	ISUPREN/CN
E24	1	ISURETIN/CN

=> s e15

L2 1 ISTRADefYLLINE/CN

=> d 12

L2 ANSWER 1 OF 1 REGISTRY COPYRIGHT 2009 ACS on STN

RN 155270-99-8 REGISTRY

ED Entered STN: 24 May 1994

CN 1H-Purine-2,6-dione, 8-[(1E)-2-(3,4-dimethoxyphenyl)ethenyl]-1,3-diethyl-

3,7-dihydro-7-methyl- (CA INDEX NAME)

OTHER CA INDEX NAMES:

CN 1H-Purine-2,6-dione, 8-[2-(3,4-dimethoxyphenyl)ethenyl]-1,3-diethyl-3,7-

dihydro-7-methyl-, (E)-

OTHER NAMES:

CN Istradefylline

CN KW 6002

FS STEREOSEARCH

MF C20 H24 N4 O4

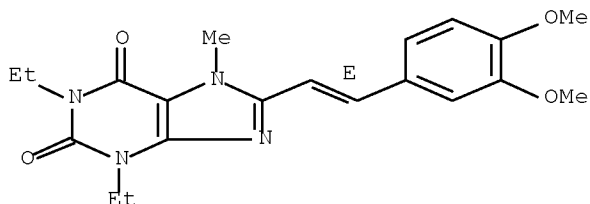
CI COM

SR CA

LC STN Files: ADISINSIGHT, ADISNEWS, AGRICOLA, BIOSIS, BIOTECHNO, CA,

CAPLUS, CASREACT, CBNB, CHEMCATS, CIN, EMBASE, IMSPATENTS,  
 IMSRESEARCH,  
 IPA, MEDLINE, PHAR, PROMT, PROUSDDR, RTECS\*, SYNTHLINE,  
 TOXCENTER, USAN,  
 USPAT2, USPATFULL  
 (\*File contains numerically searchable property data)

Double bond geometry as shown.



\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

103 REFERENCES IN FILE CA (1907 TO DATE)  
 104 REFERENCES IN FILE CAPLUS (1907 TO DATE)

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E25	1	KW 6/CN
E26	2	KW 600/CN
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E29	1	KW 6055/CN
E30	1	KW 6066N/CN
E31	1	KW 6151/CN
E32	1	KW 622/CN
E33	1	KW 6629/CN
E34	1	KW 677/CN
E35	1	KW 678/CN
E36	1	KW 7/CN

=> s e27

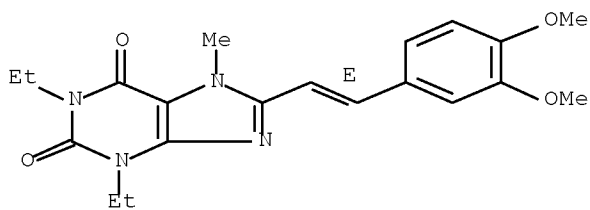
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L3 ANSWER 1 OF 1 REGISTRY COPYRIGHT 2009 ACS on STN  
 RN 155270-99-8 REGISTRY  
 ED Entered STN: 24 May 1994  
 CN 1H-Purine-2,6-dione, 8-[(1E)-2-(3,4-dimethoxyphenyl)ethenyl]-1,3-diethyl-3,7-dihydro-7-methyl- (CA INDEX NAME)  
 OTHER CA INDEX NAMES:  
 CN 1H-Purine-2,6-dione, 8-[2-(3,4-dimethoxyphenyl)ethenyl]-1,3-diethyl-3,7-

dihydro-7-methyl-, (E)-  
 OTHER NAMES:  
 CN Istradefylline  
 CN KW 6002  
 FS STEREOSEARCH  
 MF C20 H24 N4 O4  
 CI COM  
 SR CA  
 LC STN Files: ADISINSIGHT, ADISNEWS, AGRICOLA, BIOSIS, BIOTECHNO,  
 CA,  
 CAPLUS, CASREACT, CBNB, CHEMCATS, CIN, EMBASE, IMSPATENTS,  
 IMSRESEARCH,  
 IPA, MEDLINE, PHAR, PROMT, PROUSDDR, RTECS\*, SYNTHLINE,  
 TOXCENTER, USAN,  
 USPAT2, USPATFULL  
 (\*File contains numerically searchable property data)

Double bond geometry as shown.



<http://www.cas.org/legal/infopolicy.html>

This file contains CAS Registry Numbers for easy and accurate substance identification.

=> s (l1 or l2 or l3) and (brain or memory or ?cognition or apraxia or learning)

104 L1  
 104 L2  
 104 L3  
 608007 BRAIN  
 28279 BRAINS  
 611310 BRAIN  
 (BRAIN OR BRAINS)  
 179119 MEMORY  
 7454 MEMORIES  
 181248 MEMORY  
 (MEMORY OR MEMORIES)  
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 145 APRAXIA  
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 (APRAXIA OR APRAXIAS)  
 42736 LEARNING  
 105 LEARNINGS  
 42830 LEARNING

(LEARNING OR LEARNINGS)  
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 OR LEARNING)

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 22983605 PY<2003  
 4504987 AY<2003  
 3974028 PRY<2003

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L5 ANSWER 1 OF 8 CAPLUS COPYRIGHT 2009 ACS on STN  
 ACCESSION NUMBER: 2004:566535 CAPLUS Full-text  
 DOCUMENT NUMBER: 141:99728  
 TITLE: A method using  
 (E)-8-(3,4-dimethoxystyryl)-1,3-diethyl-7-  
 methylxanthine for treating behavioral  
 disorders  
 INVENTOR(S): Shiozaki, Shizuo; Shimada, Junichi; Kase,  
 Hiroshi;  
 Shindo, Mayumi  
 PATENT ASSIGNEE(S): Kyowa Hakko Kogyo Co., Ltd., Japan  
 SOURCE: PCT Int. Appl., 24 pp.  
 CODEN: PIXXD2  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004058139	A2	20040715	WO 2003-IB6455	
20031224 <--				
WO 2004058139	A3	20041104		
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CA, CH,				
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GB, GD,				
GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR,				
KZ, LC,				
LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ,				
NI, NO,				
NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL,				
SY, TJ,				
TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW,				
AM, AZ,				
BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE,				
DK, EE,				
ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE,				
SI, SK,				
TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE,				
SN, TD, TG				
CA 2511779	A1	20040715	CA 2003-2511779	

20031224 <--  
 AU 2003299432 A1 20040722 AU 2003-299432  
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 R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE,  
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 BR 2003017772 A 20051122 BR 2003-17772  
 20031224 <--  
 CN 1732005 A 20060208 CN 2003-80107517  
 20031224 <--  
 JP 2006513207 T 20060420 JP 2004-563530  
 20031224 <--  
 ZA 2005004955 A 20060426 ZA 2005-4955  
 20050617 <--  
 MX 2005006860 A 20050818 MX 2005-6860  
 20050622 <--  
 US 20060069107 A1 20060330 US 2005-539574  
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 US 20090023755 A1 20090122 US 2008-239955  
 20080929 <--  
 PRIORITY APPLN. INFO.: US 2002-509039P P  
 20021227 <--  
 WO 2003-IB6455 W  
 20031224  
 US 2005-539574 A1  
 20050728

AB The invention provides a method of treating behavioral disorders  
 such as attention deficit hyperactivity disorder, comprising  
 administering an effective amount of (E)-8-(3,4-dimethoxystyryl)-  
 1,3-diethyl-7-methylxanthine or a pharmaceutically acceptable salt  
 to a patient. This method may also be used for Tic/Tourette's  
 disorder.

TI A method using (E)-8-(3,4-dimethoxystyryl)-1,3-diethyl-7-  
 methylxanthine  
 for treating behavioral disorders

REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE  
 FOR THIS

RECORD. ALL CITATIONS AVAILABLE IN THE

RE FORMAT

PRAI US 2002-509039P P 20021227 <--  
 WO 2003-IB6455 W 20031224  
 US 2005-539574 A1 20050728

IT Brain, disease

(Gilles de la Tourette syndrome, tic/Tourette's disorder;  
 xanthine  
 derivative for treatment of behavioral disorders)

IT 155270-99-8

RL: PAC (Pharmacological activity); PRP (Properties); THU  
 (Therapeutic  
 use); BIOL (Biological study); USES (Uses)  
 (xanthine derivative for treatment of behavioral disorders)

L5 ANSWER 2 OF 8 CAPLUS COPYRIGHT 2009 ACS on STN  
 ACCESSION NUMBER: 2003:610271 CAPLUS Full-text  
 DOCUMENT NUMBER: 139:143978

TITLE: Methods using adenosine A2A receptor  
 antagonists for treating Parkinson's disease patients  
 suffering from L-DOPA/dopamine agonist therapy-associated  
 movement disorders  
 INVENTOR(S): Kase, Hiroshi; Mori, Akihisa; Waki, Yutaka;  
 Ohsawa, Yutaka; Karasawa, Akira; Kuwana, Yoshitoshi  
 PATENT ASSIGNEE(S): Japan  
 SOURCE: PCT Int. Appl., 95 pp.  
 CODEN: PIXXD2  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003063876	A2	20030807	WO 2003-US2658	
20030128 <--				
WO 2003063876	A3	20031127		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, SE, SI, SK, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2473864	A1	20030807	CA 2003-2473864	
20030128 <--				
US 20040198753	A1	20041007	US 2003-353240	
20030128 <--				
EP 1469855	A2	20041027	EP 2003-705971	
20030128 <--				
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
BR 2003006919	A	20041109	BR 2003-6919	
20030128 <--				
CN 1646132	A	20050727	CN 2003-802847	
20030128 <--				
JP 2005523898	T	20050811	JP 2003-563566	
20030128 <--				

AU 2003207734	B2	20080221	AU 2003-207734
20030128 <--			
MX 2004007299	A	20041029	MX 2004-7299
20040728 <--			
US 20060148827	A1	20060706	US 2006-326516
20060106 <--			
US 20060178379	A1	20060810	US 2006-326414
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AU 2008200611	A1	20080306	AU 2008-200611
20080208			
PRIORITY APPLN. INFO.:			US 2002-352413P P
20020128 <--			
			AU 2003-207734 A3
20030128			
			US 2003-353240 A3
20030128			
			WO 2003-US2658 W
20030128			
OTHER SOURCE(S): MARPAT 139:143978			
AB The invention provides methods for treating movement disorders by administering an effective amount of one or more adenosine A2A receptor antagonist(s) to a patient in need thereof. The invention also provides methods of decreasing the adverse effects of L-DOPA in patients receiving L-DOPA therapy in the treatment of Parkinson's disease. The invention further provides methods and compns. for treating Parkinson's disease patients with sub-clin. EDs of L-DOPA by combining L-DOPA treatment with an effective amount of one or more adenosine A2A receptor antagonists (i.e., L-DOPA sparing effect). The invention further provides methods of effective treatment of Parkinson's disease by co-administering at least one adenosine A2A receptor antagonist, L-DOPA, and a dopamine agonist and/or a COMT inhibitor and/or a MAO inhibitor. The invention further provides methods of prolonging effective treatment of Parkinson's disease by administering an adenosine A2A receptor antagonist singly or together with a dopamine agonist, and/or a COMT inhibitor, and/or a MAO inhibitor without prior or subsequent administration of L-DOPA, delaying or removing onset of L-DOPA motor complication.			
TI Methods using adenosine A2A receptor antagonists for treating Parkinson's			
disease patients suffering from L-DOPA/dopamine agonist therapy-associated			
movement disorders			
REFERENCE COUNT:	4	THERE ARE 4 CITED REFERENCES AVAILABLE	
FOR THIS		RECORD. ALL CITATIONS AVAILABLE IN THE	
RE FORMAT			
PRAI US 2002-352413P	P	20020128	<--
AU 2003-207734	A3	20030128	
US 2003-353240	A3	20030128	
WO 2003-US2658	W	20030128	
IT Brain			
(substantia nigra, pars reticulata; adenosine A2a antagonist			
for			
treating Parkinson's disease patients with L-DOPA/dopamine			
agonist			
therapy-associated motor complications)			

IT 69-89-6D, Xanthine, derivs. 322-35-0, Benserazide 155270-99-8,  
 KW 6002  
 RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL  
 (Biological study); USES (Uses)  
 (adenosine A2a antagonist for treating Parkinson's disease  
 patients  
 with L-DOPA/dopamine agonist therapy-associated motor  
 complications)

L5 ANSWER 3 OF 8 CAPLUS COPYRIGHT 2009 ACS on STN  
 ACCESSION NUMBER: 2002:793451 CAPLUS Full-text  
 DOCUMENT NUMBER: 137:289033  
 TITLE: Adenosine A2A receptor antagonists combined  
 with  
 neurotrophic activity compounds in the  
 treatment of  
 Parkinson's disease  
 INVENTOR(S): Peters, Dan; Ronn, Lars Christian; Nielsen,  
 Karin  
 Sandager  
 PATENT ASSIGNEE(S): Neurosearch A/S, Den.  
 SOURCE: PCT Int. Appl., 30 pp.  
 CODEN: PIXXD2  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002080957	A1	20021017	WO 2002-DK228	
20020404 <--				
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2440196	A1	20021017	CA 2002-2440196	
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AU 2002338309	A1	20021021	AU 2002-338309	
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EP 1379269	A1	20040114	EP 2002-759761	
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EP 1379269	B1	20090304		

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JP 2004529916 T 20040930 JP 2002-578996

20020404 <--  
US 20040097540 A1 20040520 US 2003-473809

20031002 <--  
US 7160899 B2 20070109  
MX 2003009185 A 20040217 MX 2003-9185

20031008 <--  
PRIORITY APPLN. INFO.: DK 2001-583 A

20010409 <--  
WO 2002-DK228 W

20020404 <--

AB This invention relates to the use of the combined action of a compound with neurotrophic activity and an adenosine A2A receptor antagonist for the treatment of Parkinson's disease. Adenosine A2A receptor antagonist is selected from the group consisting of KW-6002, ZM-241385, 8FB-PTP, SCH-58261, KF-17837, CGS-15943, DMPX, and pharmaceutically acceptable salts thereof. A compound with neurotrophic activity is selected from the group consisting of 5-(4-Chlorophenyl)-8-methyl-6,7,8,9-tetrahydro-1H-pyrrolo[3,2-h]isoquinoline-2,3-dione-3-oxime; 5-(4-Chlorophenyl)-6,7,8,9-tetrahydro-1H-pyrrolo[3,2-h]naphthalene-2,3-dione-3-oxime; GDNF; Neublentin; and pharmaceutically acceptable salts thereof.

TI Adenosine A2A receptor antagonists combined with neurotrophic activity

compounds in the treatment of Parkinson's disease

REFERENCE COUNT: 11 THERE ARE 11 CITED REFERENCES AVAILABLE FOR THIS

RECORD. ALL CITATIONS AVAILABLE IN THE

RE FORMAT

PI WO 2002080957 A1 20021017

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
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PI WO 2002080957	A1	20021017	WO 2002-DK228	
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GE, GH,

GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC,

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LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ,

OM, PH,

PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR,

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UA, UG, US, UZ, VN, YU, ZA, ZM, ZW

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT,

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CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT,

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BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN,

TD, TG

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     US 20040097540      A1      20040520      US 2003-473809  
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     US 7160899      B2      20070109  
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 PRAI DK 2001-583      A      20010409      <--  
     WO 2002-DK228      W      20020404      <--  
 IT    Brain  
     (nigrostriatal dopaminergic tract; adenosine A2A receptor  
 antagonists  
     combined with neurotrophic compds. in treatment of Parkinson's  
 disease)  
 IT    14114-46-6, DMPX    104615-18-1, CGS-15943    139180-30-6, ZM-241385  
     141807-96-7, KF-17837    155270-99-8, KW-6002    160098-96-4,  
     SCH-58261    160753-58-2    309711-72-6  
     RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL  
     (Biological study); USES (Uses)  
     (adenosine A2A receptor antagonists combined with neurotrophic  
 compds.  
     in treatment of Parkinson's disease)

L5    ANSWER 4 OF 8    CAPLUS    COPYRIGHT 2009 ACS on STN  
 ACCESSION NUMBER:      2002:787693    CAPLUS    Full-text  
 DOCUMENT NUMBER:      138:314421  
 TITLE:      Distribution of adenosine A2A receptor  
 antagonist  
     KW-6002 and its effect on gene expression in  
 the rat  
     brain  
 AUTHOR(S):      Aoyama, Shiro; Koga, Kumiko; Mori, Akihisa;  
 Miyaji,  
     Hiromasa; Sekine, Susumu; Kase, Hiroshi;  
 Uchimura,  
     Tatsuo; Kobayashi, Hiroyuki; Kuwana, Yoshihisa  
 CORPORATE SOURCE:      Pharmaceutical Res. Inst., Kyowa Hakko Kogyo  
 Co. Ltd.,  
     Sunto-gun, Shizuoka, 411-8731, Japan  
 SOURCE:      Brain Research (2002), 953(1,2), 119-125  
     CODEN: BRREAP; ISSN: 0006-8993  
 PUBLISHER:      Elsevier Science B.V.  
 DOCUMENT TYPE:      Journal  
 LANGUAGE:      English  
 AB    A novel adenosine A2A receptor selective antagonist, KW-6002 [(E)-  
     1,3-diethyl-8-(3,4-dimethoxystyryl)-7-methyl-3,7-dihydro-1H-  
     purine- 2,6-dione], possesses antiparkinsonian activities in  
     rodent and primate models. In the present study, the authors  
     investigated the distribution of [14C]KW-6002 in forebrain after

oral administration at pharmacol. EDs. Also, the authors monitored the effects of the compound on preproenkephalin (PPE) and preprotachykinin (PPT) gene expression in rat striatum. The highest level of radioactivity was observed in the striatum after oral administration of [<sup>14</sup>C]KW-6002; 30 min after 0.1 and 0.3 mg/kg, the d. values in the striatum were 2.45 and 2.43 times higher than those in a reference region (frontal cortex), resp. At the dose of 3 mg/kg, p.o., the ratio was only 1.58 and the compound was distributed more extensively in the brain. The distribution pattern and intensity of radioactivity were maintained even 90 min after the administration of [<sup>14</sup>C]KW-6002. Oral administration of KW-6002 (0.3 and 3 mg/kg/day) to rats for 14 days reversed the increased gene expression of PPE in striatum that had been depleted of dopamine by prior treatment with 6-hydroxydopamine (6-OHDA). On the other hand, KW-6002 did not alter the decreased gene expression of PPT in 6-OHDA-treated rats. These results are the 1st to show directly that orally administered KW-6002 is distributed selectively to the striatum and that it modulates the activity of striatopallidal enkephalin-containing neurons but not striatonigral substance P-containing neurons.

TI Distribution of adenosine A2A receptor antagonist KW-6002 and its effect

on gene expression in the rat brain

REFERENCE COUNT: 41 THERE ARE 41 CITED REFERENCES AVAILABLE FOR THIS

RECORD. ALL CITATIONS AVAILABLE IN THE

RE FORMAT

TI Distribution of adenosine A2A receptor antagonist KW-6002 and its effect

on gene expression in the rat brain

SO Brain Research (2002), 953(1,2), 119-125  
CODEN: BRREAP; ISSN: 0006-8993

AB A novel adenosine A2A receptor selective antagonist, KW-6002 [(E)-1,3-diethyl-8-(3,4-dimethoxystyryl)-7-methyl-3,7-dihydro-1H-purine-2,6-dione], possesses antiparkinsonian activities in rodent and primate models. In the present study, the authors investigated the distribution of [<sup>14</sup>C]KW-6002 in forebrain after oral administration at pharmacol. EDs. Also, the authors monitored the effects of the compound on preproenkephalin (PPE) and preprotachykinin (PPT) gene expression in rat striatum. The highest level of radioactivity was observed in the striatum after oral administration of [<sup>14</sup>C]KW-6002; 30 min after 0.1 and 0.3 mg/kg, the d. values in the striatum were 2.45 and 2.43 times higher than those in a reference region (frontal cortex), resp. At the dose of 3 mg/kg, p.o., the ratio was only 1.58 and the compound was distributed more extensively in the brain. The distribution pattern and intensity of radioactivity were maintained even 90 min after the administration of [<sup>14</sup>C]KW-6002. Oral administration of KW-6002 (0.3 and 3 mg/kg/day) to rats for 14 days reversed the increased gene expression of PPE in striatum that had been depleted of dopamine by prior treatment with 6-hydroxydopamine (6-OHDA). On the other hand, KW-6002 did not alter the decreased gene expression of PPT in 6-OHDA-treated rats. These results are the 1st to show directly that orally administered KW-6002 is distributed selectively to the striatum and that it modulates the activity of striatopallidal enkephalin-

containing neurons but not striatonigral substance P-containing neurons.

IT Adenosine receptors  
 RL: BSU (Biological study, unclassified); BIOL (Biological study)  
 (A2A, antagonist; distribution of adenosine A2A receptor antagonist  
 KW-6002 and its effect on gene expression in rat brain)

IT Brain  
 (corpus striatum; distribution of adenosine A2A receptor antagonist  
 KW-6002 and its effect on gene expression in rat brain)

IT Antiparkinsonian agents  
 Parkinson's disease  
 (distribution of adenosine A2A receptor antagonist KW-6002 and  
 its effect on gene expression in rat brain)

IT Brain  
 (forebrain; distribution of adenosine A2A receptor antagonist  
 KW-6002 and its effect on gene expression in rat brain)

IT Tachykinins  
 RL: BSU (Biological study, unclassified); BIOL (Biological study)  
 (prepro-; distribution of adenosine A2A receptor antagonist KW-6002 and  
 its effect on gene expression in rat brain)

IT 93443-35-7, Preproenkephalin  
 RL: BSU (Biological study, unclassified); BIOL (Biological study)  
 (distribution of adenosine A2A receptor antagonist KW-6002 and  
 its effect on gene expression in rat brain)

IT 155270-99-8, KW-6002  
 RL: PAC (Pharmacological activity); PKT (Pharmacokinetics); THU  
 (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (distribution of adenosine A2A receptor antagonist KW-6002 and  
 its effect on gene expression in rat brain)

L5 ANSWER 5 OF 8 CAPLUS COPYRIGHT 2009 ACS on STN  
 ACCESSION NUMBER: 2002:90903 CAPLUS Full-text  
 DOCUMENT NUMBER: 136:277364  
 TITLE: Neuroprotection by adenosine A2A receptor  
 blockade in experimental models of Parkinson's disease  
 AUTHOR(S): Ikeda, Ken; Kurokawa, Masako; Aoyama, Shiro;  
 Kuwana, Yoshihisa  
 CORPORATE SOURCE: Pharmaceutical Research Institute, Kyowa Hakko  
 Kogyo Co., Ltd., Shizuoka, 411-8731, Japan  
 SOURCE: Journal of Neurochemistry (2002), 80(2),  
 262-270  
 CODEN: JONRA9; ISSN: 0022-3042  
 PUBLISHER: Blackwell Publishing Ltd.  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English

AB Adenosine A2A receptors are abundant in the caudate-putamen and  
 involved in the motor control in several species. In MPTP-treated

monkeys, A2A receptor-blockade with an antagonist alleviates parkinsonian symptoms without provoking dyskinesia, suggesting this receptor may offer a new target for the antisymptomatic therapy of Parkinson's disease. In the present study, a significant neuroprotective effect of A2A receptor antagonists is shown in exptl. models of Parkinson's disease. Oral administration of A2A receptor antagonists protected against the loss of nigral dopaminergic neuronal cells induced by 6-hydroxydopamine in rats. A2A antagonists also prevented the functional loss of dopaminergic nerve terminals in the striatum and the ensuing gliosis caused by MPTP in mice. The neuroprotective property of A2A receptor antagonists may be exerted by altering the packaging of these neurotoxins into vesicles, thus reducing their effective intracellular concentration. We therefore conclude that the adenosine A2A receptor may provide a novel target for the long-term medication of Parkinson's disease, because blockade of this receptor exerts both acutely antisymptomatic and chronically neuroprotective activities.

TI Neuroprotection by adenosine A2A receptor blockade in experimental models

of Parkinson's disease

REFERENCE COUNT: 48 THERE ARE 48 CITED REFERENCES AVAILABLE FOR THIS

RECORD. ALL CITATIONS AVAILABLE IN THE

RE FORMAT

SO Journal of Neurochemistry (2002), 80(2), 262-270

CODEN: JONRA9; ISSN: 0022-3042

IT Brain

(corpus striatum; adenosine A2A receptor antagonist neuroprotective

property in exptl. models of Parkinson's disease)

IT Brain

(nigrostriatal dopaminergic tract; adenosine A2A receptor antagonist

neuroprotective property in exptl. models of Parkinson's disease)

IT 155270-99-8, KW-6002

RL: BSU (Biological study, unclassified); THU (Therapeutic use);

BIOL

(Biological study); USES (Uses)

(adenosine A2A receptor antagonist neuroprotective property in exptl.

models of Parkinson's disease)

L5 ANSWER 6 OF 8 CAPLUS COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 2001:864519 CAPLUS Full-text

DOCUMENT NUMBER: 136:129190

TITLE: Solubilization and immunoprecipitation of rat striatal

adenosine A2A receptors

AUTHOR(S): Harvey, Victoria; Jones, Julie; Misra, Anil; Knight,

Antony R.; Quirk, Kathleen

CORPORATE SOURCE: Department of Molecular Pharmacology, Vernalis Research Ltd., Winnersh, Wokingham, RG41 5UA,

UK

SOURCE: European Journal of Pharmacology (2001),  
431(2), 171-177  
CODEN: EJPHAZ; ISSN: 0014-2999  
PUBLISHER: Elsevier Science B.V.  
DOCUMENT TYPE: Journal  
LANGUAGE: English

AB In the present study, the authors have sought to solubilize adenosine A2A receptors from rat striatal membranes using a variety of different detergents. Of the detergents tested, 1% CHAPS yielded optimal conditions for solubilization (in the presence of 3 mg/mL protein, 44% of receptor was solubilized, 50% of total protein was solubilized). An antipeptide antibody was raised against a 15 amino-acid sequence within the predicted third intracellular loop region of the human and rat adenosine A2A receptor. The antibody was coupled to protein A immobilized on sepharose CL-4B and used to immunoppt. adenosine A2A receptors from solubilized rat striatal prepns. Radioligand-binding studies were performed using the selective adenosine A2 antagonist [3H]ZM 241385. Using [3H]ZM 241385, the pharmacol. of immunopptd. adenosine A2A receptors was composed to striatal membrane bound adenosine A2A receptors and detergent solubilized adenosine A2A receptors. [H]ZM 241385 labeled a single saturable binding site with high affinity in all three prepns. (membrane bound Kd 2.7 nM; solubilized Kd 1.9 nM; immunopptd. Kd 2.2 nM). Addnl., all three assays confirmed a rank order of potency for displacers consistent with adenosine A2A receptor pharmacol.: ZM 241385 > KW 6002 > CGS 21680 > DPCPX. The authors conclude that they have solubilized and immunopptd. adenosine A2A receptors from rat striatum and that their pharmacol. is consistent with native striatal adenosine A2A receptors.

TI Solubilization and immunoprecipitation of rat striatal adenosine A2A receptors

REFERENCE COUNT: 17 THERE ARE 17 CITED REFERENCES AVAILABLE FOR THIS

RECORD. ALL CITATIONS AVAILABLE IN THE

RE FORMAT

SO European Journal of Pharmacology (2001), 431(2), 171-177  
CODEN: EJPHAZ; ISSN: 0014-2999

IT Brain

(corpus striatum; adenosine A2A receptors of rat striatum solubilization and immunopptn.)

IT 102146-07-6, DPCPX 120225-54-9, CGS 21680 155270-99-8, KW 6002  
RL: BSU (Biological study, unclassified); BIOL (Biological study) (adenosine A2A receptors of rat striatum solubilization and immunopptn.)

L5 ANSWER 7 OF 8 CAPLUS COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 2000:637359 CAPLUS Full-text

DOCUMENT NUMBER: 134:430

TITLE: Systemic administration of adenosine A2A receptor

antagonist reverses increased GABA release in the

globus pallidus of unilateral 6-hydroxydopamine-lesioned rats: a

microdialysis study

AUTHOR(S): Ochi, M.; Koga, K.; Kurokawa, M.; Kase, H.;  
Nakamura,

J.; Kuwana, Y.

CORPORATE SOURCE: Kyowa Hakko Kogyo, Pharmaceutical Research  
Institute,

Nagaizumi, Sunto, Shizuoka, 411-8731, Japan

SOURCE: Neuroscience (Oxford) (2000), 100(1), 53-62

CODEN: NRSCDN; ISSN: 0306-4522

PUBLISHER: Elsevier Science Ltd.

DOCUMENT TYPE: Journal

LANGUAGE: English

AB The ability of adenosine A2A receptor antagonists to exhibit antiparkinsonian activity has recently been reported, but the mechanisms of action are still unknown. Since A2A receptors have been localized to GABAergic striatopallidal neurons, it is probable that these antagonists affect the activity of these neurons. In the present study, extracellular GABA basal levels were increased in the ipsilateral striatum and globus pallidus following a unilateral 6-hydroxydopamine lesion of the nigrostriatal pathway. The A2A receptor-selective antagonist KW-6002 (3 mg/kg, p.o.) caused a marked and sustained decrease of extracellular GABA levels in the globus pallidus of the 6-hydroxydopamine-lesioned rats, whereas no changes in GABA levels were observed in the globus pallidus of the non-lesioned rats. Microinjection of the A2A receptor agonist CGS21680 (0.005-0.5  $\mu$ g) into the striatum of non-lesioned animals increased GABA concns. in the globus pallidus, which was abolished by the voltage-dependent Na<sup>+</sup> channel blocker tetrodotoxin (1  $\mu$ mol/l) delivered locally to the globus pallidus via the dialysis membrane. Furthermore, intrapallidal infusion of CGS21680 (10  $\mu$ mol/l) also increased GABA levels in the globus pallidus. These data indicate that GABA release from striatopallidal neurons is regulated through A2A receptors in both the striatum and globus pallidus. The reversal of the 6-hydroxydopamine-induced increase in pallidal GABA levels by KW-6002 suggests that the antiparkinsonian effects of A2A receptor antagonists occur on the striatopallidal neurons.

TI Systemic administration of adenosine A2A receptor antagonist reverses

increased GABA release in the globus pallidus of unilateral 6-hydroxydopamine-lesioned rats: a microdialysis study

REFERENCE COUNT: 57 THERE ARE 57 CITED REFERENCES AVAILABLE FOR THIS

RECORD. ALL CITATIONS AVAILABLE IN THE

RE FORMAT

SO Neuroscience (Oxford) (2000), 100(1), 53-62

CODEN: NRSCDN; ISSN: 0306-4522

IT Brain

(corpus striatum, GABAergic system; adenosine A2A receptor antagonist

reverses increased GABA release in globus pallidus of unilateral

6-hydroxydopamine-lesioned rats)

IT Brain

(globus pallidus; adenosine A2A receptor antagonist reverses increased

GABA release in globus pallidus of unilateral

6-hydroxydopamine-lesioned rats)  
IT Brain  
(striatopallidonigral tract; adenosine A2A receptor antagonist  
reverses  
increased GABA release in globus pallidus of unilateral  
6-hydroxydopamine-lesioned rats)  
IT 155270-99-8, KW-6002  
RL: BAC (Biological activity or effector, except adverse); BSU  
(Biological  
study, unclassified); THU (Therapeutic use); BIOL (Biological  
study); USES  
(Uses)  
(adenosine A2A receptor antagonist reverses increased GABA  
release in  
globus pallidus of unilateral 6-hydroxydopamine-lesioned rats)

L5 ANSWER 8 OF 8 CAPLUS COPYRIGHT 2009 ACS on STN  
ACCESSION NUMBER: 1998:644563 CAPLUS Full-text  
DOCUMENT NUMBER: 130:33316  
TITLE: Adenosine A2A receptors modify motor function  
in  
MPTP-treated common marmosets  
AUTHOR(S): Kanda, Tomoyuki; Tashiro, Tomomi; Kuwana,  
Yoshihisa;  
Jenner, Peter  
CORPORATE SOURCE: Pharmaceutical Research Institute, Kyowa Hakko  
Kogyo  
Co Ltd, Shizuoka, 411-8731, Japan  
SOURCE: NeuroReport (1998), 9(12), 2857-2860  
CODEN: NERPEZ; ISSN: 0959-4965  
PUBLISHER: Lippincott Williams & Wilkins  
DOCUMENT TYPE: Journal  
LANGUAGE: English

AB Both adenosine A1 and A2 receptor populations are located in the  
striatum and can modify locomotor activity, and they may form a  
therapeutic target for Parkinson's disease (PD). Administration  
of the selective adenosine A2A antagonist (E)-1,3-diethyl-8-(3,4-  
dimethoxystyryl)-7-methyl-3,7- dihydro-1H-purine-2,6-dione (KW-  
6002) to MPTP-treated common marmosets increased locomotor  
activity. In contrast, administration of the selective A1  
receptor antagonist 1,3-dipropyl-8-cyclopentylxanthine (DPCPX) had  
no effect on locomotion. Administration of the adenosine A2A  
receptor agonist 2-[p-[2-(2-aminoethylamino) carbonylethyl]  
phenethyl amino]-5'-N-ethylcarboxamidoadenosine (APEC) dose  
dependently suppressed basal locomotor activity. A minimally ED  
of APEC (0.62 mg/kg, i.p) completely reversed the increase in  
locomotor activity produced by administration of KW-6002. The  
adenosine A2A receptor appears to be an important target for the  
treatment of basal ganglia disorders, particularly PD.

TI Adenosine A2A receptors modify motor function in MPTP-treated  
common  
marmosets

REFERENCE COUNT: 18 THERE ARE 18 CITED REFERENCES AVAILABLE  
FOR THIS

RECORD. ALL CITATIONS AVAILABLE IN THE

RE FORMAT

SO NeuroReport (1998), 9(12), 2857-2860

CODEN: NERPEZ; ISSN: 0959-4965

IT Brain, disease  
 (basal ganglion; adenosine A2A receptors modify motor function  
 in  
 MPTP-treated common marmoset Parkinsonism model)

IT Brain  
 (corpus striatum; adenosine A2A receptors modify motor function  
 in  
 MPTP-treated common marmoset Parkinsonism model)

IT 155270-99-8  
 RL: BAC (Biological activity or effector, except adverse); BSU  
 (Biological  
 study, unclassified); THU (Therapeutic use); BIOL (Biological  
 study); USES  
 (Uses)  
 (adenosine A2A receptors modify motor function in MPTP-treated  
 common  
 marmoset Parkinsonism model)

=> s (l1 or l2 or l3) and (memory or ?cognition or apraxia or  
 learning)

104 L1  
 104 L2  
 104 L3  
 179119 MEMORY  
 7454 MEMORIES  
 181248 MEMORY  
 (MEMORY OR MEMORIES)  
 165227 ?COGNITION  
 145 APRAXIA  
 1 APRAXIAS  
 145 APRAXIA  
 (APRAXIA OR APRAXIAS)  
 42736 LEARNING  
 105 LEARNINGS  
 42830 LEARNING  
 (LEARNING OR LEARNINGS)

L6 3 (L1 OR L2 OR L3) AND (MEMORY OR ?COGNITION OR APRAXIA  
 OR LEARNI  
 NG)

=> d l6 ibib abs ti hit 1-3

L6 ANSWER 1 OF 3 CAPLUS COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 2008:446836 CAPLUS Full-text

DOCUMENT NUMBER: 149:462747

TITLE: Adenosine A2A receptor blockade prevents  
 memory dysfunction caused by  $\beta$ -amyloid  
 peptides but not by scopolamine or MK-801

AUTHOR(S): Cunha, Geanne M. A.; Canas, Paula M.; Melo,  
 Carolina  
 S.; Hockemeyer, Joerg; Mueller, Christa E.;  
 Oliveira,  
 Catarina R.; Cunha, Rodrigo A.

CORPORATE SOURCE: Center for Neuroscience of Coimbra, Institute  
 of

of Biochemistry, Faculty of Medicine, University  
Coimbra, Coimbra, 3004-504, Port.  
SOURCE: Experimental Neurology (2008), 210(2), 776-781  
CODEN: EXNEAC; ISSN: 0014-4886  
PUBLISHER: Elsevier  
DOCUMENT TYPE: Journal  
LANGUAGE: English

AB Adenosine A2A receptor antagonists alleviate memory deficits caused by aging or by administration of  $\beta$ -amyloid peptides in rodents, which is in accordance with the beneficial effects of caffeine consumption (an adenosine receptor antagonist) on memory performance in aged individuals and in preventing Alzheimer's disease. We now tested if A2A receptor blockade affords a general beneficial effect in different exptl. paradigms disturbing memory performance in rodents. The  $\beta$ -amyloid fragment present in patients with Alzheimer's disease (A $\beta$ 1-42, 2 nmol, icv) decreased spontaneous alternation in the Y-maze after 15 days (29%) to an extent similar to the decrease of memory performance caused by scopolamine (2 mg/kg, i.p.) or MK-801 (0.25 mg/kg, i.p.) after 30 min (28% and 39%, resp.). The selective A2A receptor antagonist SCH58261 (0.05 mg/kg, i.p. every 24 h, starting 30 min before the noxious stimuli) prevented A $\beta$ 1-42-induced amnesia, but failed to modify scopolamine- or MK-801-induced amnesia. Similar conclusions were reached when testing another A2A receptor antagonist (KW6002, 3 mg/kg, i.p.). These results indicate that A2A receptors do not affect general processes of memory impairment but instead play a crucial role restricted to neurodegenerative conditions involving an insidious synaptic deterioration leading to memory dysfunction.

TI Adenosine A2A receptor blockade prevents memory dysfunction caused by  $\beta$ -amyloid peptides but not by scopolamine or MK-801

REFERENCE COUNT: 35 THERE ARE 35 CITED REFERENCES AVAILABLE FOR THIS

RECORD. ALL CITATIONS AVAILABLE IN THE

RE FORMAT

TI Adenosine A2A receptor blockade prevents memory dysfunction caused by  $\beta$ -amyloid peptides but not by scopolamine or MK-801

AB Adenosine A2A receptor antagonists alleviate memory deficits caused by aging or by administration of  $\beta$ -amyloid peptides in rodents, which is in accordance with the beneficial effects of caffeine consumption (an adenosine receptor antagonist) on memory performance in aged individuals and in preventing Alzheimer's disease. We now tested if A2A receptor blockade affords a general beneficial effect in different exptl. paradigms disturbing memory performance in rodents. The  $\beta$ -amyloid fragment present in patients with Alzheimer's disease (A $\beta$ 1-42, 2 nmol, icv) decreased spontaneous alternation in the Y-maze after 15 days (29%) to an extent similar to the decrease of memory performance caused by scopolamine (2 mg/kg, i.p.) or MK-801 (0.25 mg/kg, i.p.) after 30 min (28% and 39%, resp.). The selective A2A receptor antagonist SCH58261 (0.05 mg/kg, i.p. every 24 h, starting 30 min before the noxious stimuli) prevented A $\beta$ 1-42-induced amnesia, but failed to modify scopolamine- or MK-801-induced amnesia. Similar conclusions were reached when testing another A2A receptor

antagonist (KW6002, 3 mg/kg, i.p.). These results indicate that A2A receptors do not affect general processes of memory impairment but instead play a crucial role restricted to neurodegenerative conditions involving an insidious synaptic deterioration leading to memory dysfunction.

L6 ANSWER 2 OF 3 CAPLUS COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 2007:588263 CAPLUS Full-text

DOCUMENT NUMBER: 147:378757

TITLE: The effect of striatal dopamine depletion and the

adenosine A2A antagonist KW-6002 on reversal learning in rats

AUTHOR(S): O'Neill, Martin; Brown, Verity J.

CORPORATE SOURCE: School of Psychology, University of St. Andrews,

Scotland, KY16 9JU, UK

SOURCE: Neurobiology of Learning and Memory (2007), 88(1),

75-81

CODEN: NLMEFR; ISSN: 1074-7427

PUBLISHER: Elsevier B.V.

DOCUMENT TYPE: Journal

LANGUAGE: English

AB This study assessed whether dopamine in the dorsomedial striatum is necessary for flexible adaptation to changes in stimulus-response contingencies. As KW-6002 (Istradefylline), an adenosine A2A antagonist, improves motor deficits resulting from striatal dopamine depletion, we also tested for potential ameliorative effects of KW-6002 on dopamine depletion-induced cognitive deficits. Male Lister hooded rats were presented with two bowls, discriminable by either a textured covering on the outer surface, their scent or the bowl contents (digging media) in which bait was buried. Once they had learned in which bowl food was buried, the stimulus-response contingencies were reversed. In both phases (acquisition and reversal), the criterion for learning was defined a priori as six consecutive correct trials. Following depletion of dopamine in the dorsomedial striatum, acquisition of the discriminations was intact but there was an increase in the number of trials to attain criterion performance in the reversal phases, indicating an impairment in reversal learning. KW-6002 (1 mg/kg bidaily for 10 days) non-specifically increased the number of trials to criterion at all stages of the test and in both controls (sham-operated) and dopamine-depleted rats. Chronic KW-6002 treatment did not improve the reversal deficits in dopamine-depleted rats. These findings suggest that dopamine transmission in the dorsomedial striatum is critical for the flexible shifting of response patterns and the ameliorative effects of KW-6002 following depletion of dopamine in the striatum may be restricted to motor functions without relieving deficits in response-shifting flexibility.

TI The effect of striatal dopamine depletion and the adenosine A2A antagonist

KW-6002 on reversal learning in rats

REFERENCE COUNT: 46 THERE ARE 46 CITED REFERENCES AVAILABLE FOR THIS

RECORD. ALL CITATIONS AVAILABLE IN THE

RE FORMAT

TI The effect of striatal dopamine depletion and the adenosine A2A antagonist  
KW-6002 on reversal learning in rats

L6 ANSWER 3 OF 3 CAPLUS COPYRIGHT 2009 ACS on STN  
ACCESSION NUMBER: 2005:547543 CAPLUS Full-text

DOCUMENT NUMBER: 143:53542

TITLE: Xanthine derivatives and salts and compositions for

dysfunction preventing and/or treating higher brain

INVENTOR(S): Kase, Hiroshi; Nakagawa, Yutaka; Shiozaki, Shizuo;

Naoki; Kobayashi, Minoru; Toki, Shinichiro; Seno,

Ikeda, Ken

PATENT ASSIGNEE(S): Kyowa Hakko Kogyo Co., Ltd., Japan

SOURCE: PCT Int. Appl., 29 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: Japanese

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO. -----	KIND ----	DATE -----	APPLICATION NO. -----	DATE ----
WO 2005056016 20041209	A1	20050623	WO 2004-JP18765	
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2004296137 20041209	A1	20050623	AU 2004-296137	
CA 2550130 20041209	A1	20050623	CA 2004-2550130	
EP 1709966 20041209	A1	20061011	EP 2004-807124	

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE,  
MC, PT,

IE, SI, LT, FI, RO, CY, TR, BG, CZ, EE, HU, PL, SK, IS  
CN 1889959 A 20070103 CN 2004-80036267

20041209

BR 2004017241 A 20070306 BR 2004-17241

20041209

US 20070078148 A1 20070405 US 2006-579829

20060517

MX 2006005965 A 20060809 MX 2006-5965

20060525

KR 2006124615 A 20061205 KR 2006-711123

20060607

IN 2006CN02490 A 20070608 IN 2006-CN2490

20060706

PRIORITY APPLN. INFO.: JP 2003-410432 A

20031209

WO 2004-JP18765 W

20041209

OTHER SOURCE(S): MARPAT 143:53542

AB A preventive and/or therapeutic agent for higher brain  
dysfunctions which contains as an active ingredient a xanthine  
derivative represented, for example, by the following formula (I)  
or a pharmacol. acceptable salt thereof: (I) (II) wherein R1, R2,  
and R3 are the same or different and each represents hydrogen,  
lower alkyl, lower alkenyl, or lower alkynyl; R4 represents  
cycloalkyl, -(CH2)n-R5, or the formula (II) given above; and X1  
and X2 are the same or different and each represents oxygen or  
sulfur. The higher brain dysfunction includes aging brain damage,  
brain trauma, cerebrovascular disease, memory disorder, thinking  
disorder, recognition disorder, behavior disorder, learning  
disorder, etc.

TI Xanthine derivatives and salts and compositions for preventing  
and/or

treating higher brain dysfunction

<http://www.cas.org/support/stngen/stndoc/properties.html>

=> e 141807-96-7/rn

E37 1 141807-94-5/RN

E38 1 141807-95-6/RN

E39 1 --> 141807-96-7/RN

E40 1 141807-97-8/RN

E41 1 141807-98-9/RN

E42 1 141807-99-0/RN

E43 1 141808-00-6/RN

E44 1 141808-01-7/RN

E45 1 141808-02-8/RN

E46 1 141808-03-9/RN

E47 1 141808-04-0/RN

E48 1 141808-05-1/RN

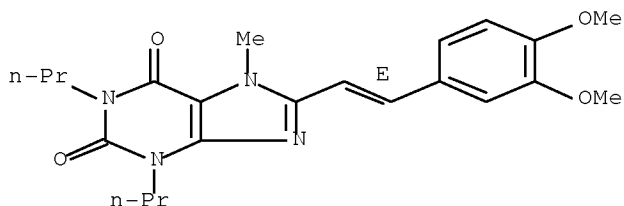
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L7 1 141807-96-7/RN

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L7 ANSWER 1 OF 1 REGISTRY COPYRIGHT 2009 ACS on STN  
 RN 141807-96-7 REGISTRY  
 ED Entered STN: 12 Jun 1992  
 CN 1H-Purine-2,6-dione, 8-[(1E)-2-(3,4-dimethoxyphenyl)ethenyl]-3,7-dihydro-7-methyl-1,3-dipropyl- (CA INDEX NAME)  
 OTHER CA INDEX NAMES:  
 CN 1H-Purine-2,6-dione, 8-[2-(3,4-dimethoxyphenyl)ethenyl]-3,7-dihydro-7-methyl-1,3-dipropyl-, (E)-  
 OTHER NAMES:  
 CN KF 17837  
 CN KW 17837  
 FS STEREOSEARCH  
 MF C22 H28 N4 O4  
 SR CA  
 LC STN Files: ADISINSIGHT, BEILSTEIN\*, BIOSIS, BIOTECHNO, CA, CAPLUS, EMBASE, IMSDRUGNEWS, IMSRESEARCH, PROUSDDR, RTECS\*, TOXCENTER, USPAT2, USPATFULL  
 (\*File contains numerically searchable property data)

Double bond geometry as shown.



\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

55 REFERENCES IN FILE CA (1907 TO DATE)  
 55 REFERENCES IN FILE CAPLUS (1907 TO DATE)

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 E50 1 155271-99-1/RN  
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 E53 1 155272-02-9/RN  
 E54 1 155272-03-0/RN  
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 E56 1 155272-05-2/RN  
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 E58 1 155272-07-4/RN  
 E59 1 155272-08-5/RN  
 E60 1 155272-09-6/RN

=> s e51

L8 1 155272-00-7/RN

=> d 18

L8 ANSWER 1 OF 1 REGISTRY COPYRIGHT 2009 ACS on STN

RN 155272-00-7 REGISTRY

ED Entered STN: 24 May 1994

CN 1H-Purine-2,6-dione, 1,3-diethyl-3,7-dihydro-8-[(1E)-2-(7-methoxy-1,3-

benzodioxol-5-yl)ethenyl]-7-methyl- (CA INDEX NAME)

OTHER CA INDEX NAMES:

CN 1H-Purine-2,6-dione, 1,3-diethyl-3,7-dihydro-8-[2-(7-methoxy-1,3-benzodioxol-5-yl)ethenyl]-7-methyl-, (E)-

OTHER NAMES:

CN (E)-1,3-Diethyl-8-(3,4-methylenedioxy-5-methoxystyryl)-7-methylxanthine

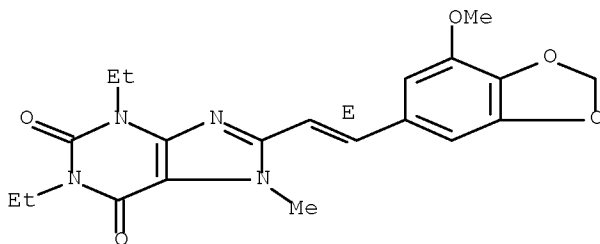
FS STEREOSEARCH

MF C20 H22 N4 O5

SR CA

LC STN Files: CA, CAPLUS, RTECS\*, TOXCENTER, USPAT2, USPATFULL  
(\*File contains numerically searchable property data)

Double bond geometry as shown.



\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

8 REFERENCES IN FILE CA (1907 TO DATE)

8 REFERENCES IN FILE CAPLUS (1907 TO DATE)

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E67 1 51389-41-4/RN

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E70 1 51389-44-7/RN

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E72 1 51389-46-9/RN

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=> s e63

L9 1 51389-37-8/RN

=> d 19

L9 ANSWER 1 OF 1 REGISTRY COPYRIGHT 2009 ACS on STN

RN 51389-37-8 REGISTRY

ED Entered STN: 16 Nov 1984

CN 1H-Purine-2,6-dione, 3,7-dihydro-1,3,7-trimethyl-8-[(1E)-2-(3,4,5-trimethoxyphenyl)ethenyl]- (CA INDEX NAME)

OTHER CA INDEX NAMES:

CN 1H-Purine-2,6-dione, 3,7-dihydro-1,3,7-trimethyl-8-[2-(3,4,5-trimethoxyphenyl)ethenyl]-, (E)-

OTHER NAMES:

CN KF 18446

CN trans-8-(3,4,5-Trimethoxystyryl)caffeine

FS STEREOSEARCH

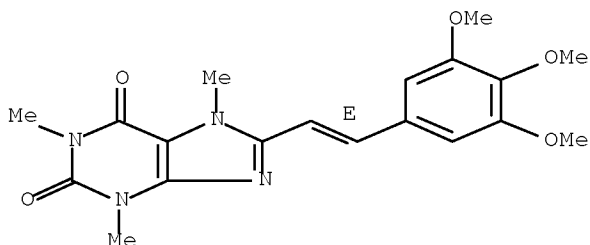
MF C19 H22 N4 O5

LC STN Files: BEILSTEIN\*, BIOSIS, CA, CAPLUS, RTECS\*, TOXCENTER, USPAT2,

USPATFULL

(\*File contains numerically searchable property data)

Double bond geometry as shown.



\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

14 REFERENCES IN FILE CA (1907 TO DATE)

14 REFERENCES IN FILE CAPLUS (1907 TO DATE)

=> e 69-89-6/rn

E73 1 69-81-8/RN

E74 1 69-86-3/RN

E75 1 --> 69-89-6/RN

E76 1 69-90-9/RN

E77 1 69-91-0/RN

E78 1 69-93-2/RN

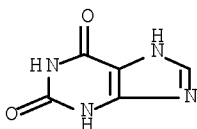
E79 1 69-96-5/RN  
E80 1 690-00-6/RN  
E81 1 690-01-7/RN  
E82 1 690-02-8/RN  
E83 1 690-03-9/RN  
E84 1 690-04-0/RN

=> s e75

L10 1 69-89-6/RN

=> d l10

L10 ANSWER 1 OF 1 REGISTRY COPYRIGHT 2009 ACS on STN  
RN ~~69-89-6~~ REGISTRY  
ED Entered STN: 16 Nov 1984  
CN 1H-Purine-2,6-dione, 3,9-dihydro- (CA INDEX NAME)  
OTHER CA INDEX NAMES:  
CN 1H-Purine-2,6-dione, 3,7-dihydro- (9CI)  
CN Xanthine (8CI)  
OTHER NAMES:  
CN 1H,3H,7H-Xanthine  
CN 1H,3H,9H-Xanthine  
CN 1H-Purine-2,6-diol  
CN 2,6-Dioxo-1,2,3,6-tetrahydropurine  
CN 2,6-Dioxopurine  
CN 3,9-Dihydro-1H-purine-2,6-dione  
CN 3,9-Dihydropurine-2,6-dione  
CN 9H-Purine-2,6(1H,3H)-dione  
CN Isoxanthine  
CN NSC 14664  
CN Pseudoxanthine  
CN Purine-2,6(1H,3H)-dione  
CN Xan  
CN Xanthic oxide  
CN Xanthin  
DR 16819-86-6, 51953-26-5, 6050-36-8, 6053-41-4, 28522-58-9, 33669-  
67-9,  
42911-15-9  
MF C5 H4 N4 O2  
CI COM  
LC STN Files: ADISNEWS, AGRICOLA, ANABSTR, BEILSTEIN\*, BIOSIS,  
BIOTECHNO,  
CA, CABA, CAPLUS, CASREACT, CBNB, CHEMCATS, CHEMINFORMRX,  
CHEMLIST, CIN,  
CSCHEM, DDFU, DETHERM\*, DRUGU, EMBASE, GMELIN\*, IFICDB, IFIPAT,  
IFIUDB,  
IPA, MEDLINE, MRCK\*, MSDS-OHS, NAPRALERT, PIRA, PROMT, RTECS\*,  
SPECINFO,  
TOXCENTER, USPAT2, USPATFULL, USPATOLD  
(\*File contains numerically searchable property data)  
Other Sources: DSL\*\*, EINECS\*\*, TSCA\*\*  
(\*\*Enter CHEMLIST File for up-to-date regulatory information)



\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

5562 REFERENCES IN FILE CA (1907 TO DATE)  
 926 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA  
 5581 REFERENCES IN FILE CAPLUS (1907 TO DATE)

=> e kf 18446/cn

E85	1	KF 18259/CN
E86	1	KF 18280/CN
E87	1 -->	KF 18446/CN
E88	1	KF 18627/CN
E89	1	KF 1935/CN
E90	1	KF 19418/CN
E91	1	KF 19514/CN
E92	1	KF 19631/CN
E93	1	KF 1M/CN
E94	1	KF 1X4/CN
E95	2	KF 2/CN
E96	1	KF 2 (FLUX)/CN

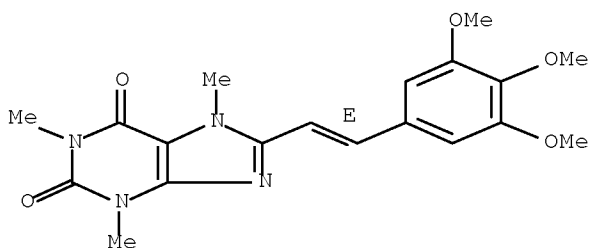
=> s e87

L11 1 "KF 18446"/CN

=> d l11

L11 ANSWER 1 OF 1 REGISTRY COPYRIGHT 2009 ACS on STN  
 RN 51389-37-8 REGISTRY  
 ED Entered STN: 16 Nov 1984  
 CN 1H-Purine-2,6-dione, 3,7-dihydro-1,3,7-trimethyl-8-[(1E)-2-(3,4,5-trimethoxyphenyl)ethenyl]- (CA INDEX NAME)  
 OTHER CA INDEX NAMES:  
 CN 1H-Purine-2,6-dione, 3,7-dihydro-1,3,7-trimethyl-8-[2-(3,4,5-trimethoxyphenyl)ethenyl]-, (E)-  
 OTHER NAMES:  
 CN KF 18446  
 CN trans-8-(3,4,5-Trimethoxystyryl)caffeine  
 FS STEREOSEARCH  
 MF C19 H22 N4 O5  
 LC STN Files: BEILSTEIN\*, BIOSIS, CA, CAPLUS, RTECS\*, TOXCENTER, USPAT2,  
 USPATFULL  
 (\*File contains numerically searchable property data)

Double bond geometry as shown.



\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

14 REFERENCES IN FILE CA (1907 TO DATE)

14 REFERENCES IN FILE CAPLUS (1907 TO DATE)

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E97	1	KF 17625/CN
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E99	1 -->	KF 17837/CN
E100	1	KF 17837S/CN
E101	1	KF 18259/CN
E102	1	KF 18280/CN
E103	1	KF 18446/CN
E104	1	KF 18627/CN
E105	1	KF 1935/CN
E106	1	KF 19418/CN
E107	1	KF 19514/CN
E108	1	KF 19631/CN

=> s e99

L12 1 "KF 17837"/CN

=> d l12

L12 ANSWER 1 OF 1 REGISTRY COPYRIGHT 2009 ACS on STN

RN 141807-96-7 REGISTRY

ED Entered STN: 12 Jun 1992

CN 1H-Purine-2,6-dione, 8-[(1E)-2-(3,4-dimethoxyphenyl)ethenyl]-3,7-dihydro-7-

methyl-1,3-dipropyl- (CA INDEX NAME)

OTHER CA INDEX NAMES:

CN 1H-Purine-2,6-dione, 8-[2-(3,4-dimethoxyphenyl)ethenyl]-3,7-dihydro-7-

methyl-1,3-dipropyl-, (E)-

OTHER NAMES:

CN KF 17837

CN KW 17837

FS STEREOSEARCH

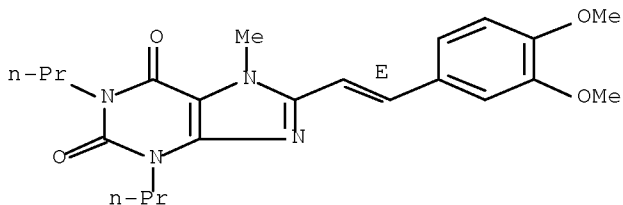
MF C22 H28 N4 O4

SR CA

LC STN Files: ADISINSIGHT, BEILSTEIN\*, BIOSIS, BIOTECHNO, CA, CAPLUS,

EMBASE, IMSDRUGNEWS, IMSRESEARCH, PROUSDDR, RTECS\*, TOXCENTER,  
 USPAT2,  
 USPATFULL  
 (\*File contains numerically searchable property data)

Double bond geometry as shown.



\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

55 REFERENCES IN FILE CA (1907 TO DATE)  
 55 REFERENCES IN FILE CAPLUS (1907 TO DATE)

=> e kw 17837/cn

E109	1	KW 139/CN
E110	1	KW 1539/CN
E111	1 -->	KW 17837/CN
E112	1	KW 1937/CN
E113	1	KW 1938/CN
E114	1	KW 1976/CN
E115	1	KW 2/CN
E116	1	KW 2000/CN
E117	1	KW 2007/CN
E118	1	KW 2030/CN
E119	1	KW 2083/CN
E120	1	KW 2100/CN

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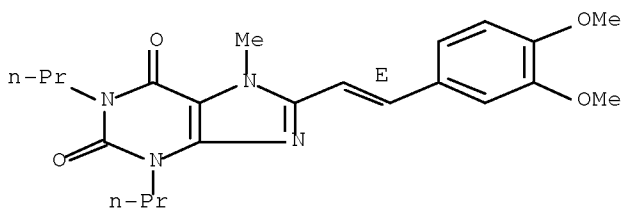
L13 1 "KW 17837"/CN

=> d 113

L13 ANSWER 1 OF 1 REGISTRY COPYRIGHT 2009 ACS on STN  
 RN 141807-96-7 REGISTRY  
 ED Entered STN: 12 Jun 1992  
 CN 1H-Purine-2,6-dione, 8-[(1E)-2-(3,4-dimethoxyphenyl)ethenyl]-3,7-dihydro-7-methyl-1,3-dipropyl- (CA INDEX NAME)  
 OTHER CA INDEX NAMES:  
 CN 1H-Purine-2,6-dione, 8-[2-(3,4-dimethoxyphenyl)ethenyl]-3,7-dihydro-7-methyl-1,3-dipropyl-, (E)-  
 OTHER NAMES:  
 CN KF 17837  
 CN KW 17837

FS STEREOSEARCH  
 MF C22 H28 N4 O4  
 SR CA  
 LC STN Files: ADISINSIGHT, BEILSTEIN\*, BIOSIS, BIOTECHNO, CA,  
 CAPLUS,  
 EMBASE, IMSDRUGNEWS, IMSRESEARCH, PROUSDDR, RTECS\*, TOXCENTER,  
 USPAT2,  
 USPATFULL  
 (\*File contains numerically searchable property data)

Double bond geometry as shown.



This file contains CAS Registry Numbers for easy and accurate substance identification.

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=> s (17 or 19 or 111 or 112 or 113)
      55 L7
      14 L9
      14 L11
      55 L12
      55 L13
L14      58 (L7 OR L9 OR L11 OR L12 OR L13)
  
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=> s 114 and brain, disease/it
      495101 BRAIN/IT
      2040 BRAINS/IT
      495220 BRAIN/IT
            ((BRAIN OR BRAINS)/IT)
      867672 DISEASE/IT
      105349 DISEASES/IT
      913630 DISEASE/IT
            ((DISEASE OR DISEASES)/IT)
      71978 BRAIN, DISEASE/IT
            ((BRAIN(W)DISEASE)/IT)
L15      1 L14 AND BRAIN, DISEASE/IT
  
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=> s 114 and learning disorders/it
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      4 LEARNINGS/IT
      18470 LEARNING/IT
            ((LEARNING OR LEARNINGS)/IT)
      145760 DISORDERS/IT
      1263 LEARNING DISORDERS/IT
            ((LEARNING(W)DISORDERS)/IT)
L16      1 L14 AND LEARNING DISORDERS/IT
  
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=> s 114 and mental and behavioral disorders/it
  
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        66412 MENTAL
            5 MENTALS
        66416 MENTAL
            (MENTAL OR MENTALS)
        31717 BEHAVIORAL/IT
        31717 BEHAVIORAL/IT
            ((BEHAVIORAL OR BEHAVIOURAL)/IT)
        145760 DISORDERS/IT
        20949 BEHAVIORAL DISORDERS/IT
            ((BEHAVIORAL(W)DISORDERS)/IT)
L17          2 L14 AND MENTAL AND BEHAVIORAL DISORDERS/IT

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            1779 MEMORIES/IT
        104686 MEMORY/IT
            ((MEMORY OR MEMORIES)/IT)
        3903901 BIOLOGICAL/IT
            537 BIOLOGICALS/IT
        3904271 BIOLOGICAL/IT
            ((BIOLOGICAL OR BIOLOGICALS)/IT)
        246352 BIOL/IT
            12 BIOLS/IT
        246362 BIOL/IT
            ((BIOL OR BIOLS)/IT)
        4062690 BIOLOGICAL/IT
            ((BIOLOGICAL OR BIOL)/IT)
        18207 MEMORY, BIOLOGICAL/IT
            ((MEMORY(W)BIOLOGICAL)/IT)
L18          1 L14 AND MEMORY, BIOLOGICAL/IT

=> s l14 and (learning or amnesia or dopamin? or motor? or ?acognit?)
        42736 LEARNING
            105 LEARNINGS
        42830 LEARNING
            (LEARNING OR LEARNINGS)
        3941 AMNESIA
            23 AMNESIAS
        3945 AMNESIA
            (AMNESIA OR AMNESIAS)
        108298 DOPAMIN?
        152363 MOTOR?
        367914 ENGINE?
        507815 MOTOR?
            (MOTOR? OR ENGINE?)
            70 ?ACOGNIT?
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?ACOGNIT?)

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        4504987 AY<2003
        3974028 PRY<2003
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L20 ANSWER 1 OF 6 CAPLUS COPYRIGHT 2009 ACS on STN  
ACCESSION NUMBER: 2004:570030 CAPLUS Full-text

DOCUMENT NUMBER: 141:99661

TITLE: Identification of compounds suitable as  
agonists

and/or antagonists of adenosine A2A receptor

coupled

to specific G proteins, and use of identified  
compounds in treatment of various disorders in

mammals

INVENTOR(S): Fredholm, Bertil B.; Kull, Bjoern

PATENT ASSIGNEE(S): Actar Ab, Swed.

SOURCE: PCT Int. Appl., 22 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
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WO 2004058974	A1	20040715	WO 2003-SE2086	
20031229 <--				
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RW:	GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG			
AU 2003291608	A1	20040722	AU 2003-291608	
20031229 <--				
PRIORITY APPLN. INFO.:			US 2002-436480P	P
20021227 <--				
			WO 2003-SE2086	W

20031229

AB The invention discloses a method of drug screening to select chemical compds. suitable as receptor agonists or antagonists that act on a receptor belonging to the family of G protein coupled receptors. The method involves constructing a biol. preparation comprising a receptor coupled to a specific G protein, bringing a compound in contact with said preparation, and studying the functional properties of said compound in biol. preparation The invention also discloses the use of identified compound as a drug

for treatment of CNS disorders, cardiovascular disorders, inflammatory disorders, metabolic disorders, cancer and other hyperproliferative disorders in a mammal. Specifically, the invention discloses a novel approach to identify and test compds. based on changes in adenosine A2A receptor binding dependent on the nature of the coupled G protein. The invention related that this approach seemed feasible due to the evidence that G proteins, such as Gs, Gi or Golf, influence the binding properties of A2A receptors. The invention also related that a truly efficient drug mol., in addition to affinity towards A2A, can be specific towards the different G proteins associated with A2A. In the examples, the invention used transformed CHO cells expressing A2A receptors linked to Gs or Golf G proteins, and demonstrated the existence of G-protein-dependent ligand specificity. Specifically, the examples demonstrated that substance KF 17837 has higher affinity to the A2A-Golf complex in striatum than to A2A-Gs complex in leukocytes. The examples also showed how some compds. influence A2A receptors coupled to Golf more readily than A2A receptors coupled to Gs.

TI Identification of compounds suitable as agonists and/or antagonists of

adenosine A2A receptor coupled to specific G proteins, and use of identified compounds in treatment of various disorders in mammals

REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS

RECORD. ALL CITATIONS AVAILABLE IN THE

RE FORMAT

PRAI US 2002-436480P P 20021227 <--  
WO 2003-SE2086 W 20031229

IT Central nervous system, disease

(dopamine-related; method of drug screening to select

agonists or antagonists of G protein coupled receptors, and use

of

identified drug in treatment of various disorders including)

IT 51-61-6, Dopamine, biological studies

RL: BSU (Biological study, unclassified); BIOL (Biological study)

(method of drug screening to select agonists or antagonists of

G

protein coupled receptors, and use of identified drug in

treatment of

various disorders including dopamine-related CNS disorders)

IT 141807-96-7, KF 17837

RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL

(Biological study); USES (Uses)

(substance KF 17837 has higher affinity to A2A receptor -Golf

complex

in striatum than to A2A-Gs complex in leukocytes)

L20 ANSWER 2 OF 6 CAPLUS COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 2002:793451 CAPLUS Full-text

DOCUMENT NUMBER: 137:289033

TITLE: Adenosine A2A receptor antagonists combined  
with

neurotrophic activity compounds in the

treatment of

Parkinson's disease

INVENTOR(S): Peters, Dan; Ronn, Lars Christian; Nielsen,

Karin

PATENT ASSIGNEE(S): Sandager  
SOURCE: Neurosearch A/S, Den.  
PCT Int. Appl., 30 pp.  
CODEN: PIXXD2  
DOCUMENT TYPE: Patent  
LANGUAGE: English  
FAMILY ACC. NUM. COUNT: 1  
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
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WO 2002080957	A1	20021017	WO 2002-DK228	
20020404 <--				
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA,				
CH, CN,				
CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD,				
GE, GH,				
GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC,				
LK, LR,				
LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ,				
OM, PH,				
PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR,				
TT, TZ,				
UA, UG, US, UZ, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT,				
BE, CH,				
CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT,				
SE, TR,				
BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN,				
TD, TG				
CA 2440196	A1	20021017	CA 2002-2440196	
20020404 <--				
AU 2002338309	A1	20021021	AU 2002-338309	
20020404 <--				
EP 1379269	A1	20040114	EP 2002-759761	
20020404 <--				
EP 1379269	B1	20090304		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE,				
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IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
JP 2004529916	T	20040930	JP 2002-578996	
20020404 <--				
US 20040097540	A1	20040520	US 2003-473809	
20031002 <--				
US 7160899	B2	20070109		
MX 2003009185	A	20040217	MX 2003-9185	
20031008 <--				
PRIORITY APPLN. INFO.:			DK 2001-583	A
20010409 <--				
			WO 2002-DK228	W
20020404 <--				

AB This invention relates to the use of the combined action of a compound with neurotrophic activity and an adenosine A2A receptor antagonist for the treatment of Parkinson's disease. Adenosine A2A receptor antagonist is selected from the group consisting of

KW-6002, ZM-241385, 8FB-PTP, SCH-58261, KF-17837, CGS-15943, DMPX, and pharmaceutically acceptable salts thereof. A compound with neurotrophic activity is selected from the group consisting of 5-(4-Chlorophenyl)-8-methyl-6,7,8,9-tetrahydro-1H-pyrrolo[3,2-h]isoquinoline-2,3-dione-3-oxime; 5-(4-Chlorophenyl)-6,7,8,9-tetrahydro-1H-pyrrolo[3,2-h]naphthalene-2,3-dione-3-oxime; GDNF; Neublentin; and pharmaceutically acceptable salts thereof.

TI Adenosine A2A receptor antagonists combined with neurotrophic activity

compounds in the treatment of Parkinson's disease

REFERENCE COUNT: 11 THERE ARE 11 CITED REFERENCES AVAILABLE FOR THIS

RECORD. ALL CITATIONS AVAILABLE IN THE

RE FORMAT

PI WO 2002080957 A1 20021017

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
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PI WO 2002080957 A1 20021017 WO 2002-DK228

20020404 <--

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

CA 2440196 A1 20021017 CA 2002-2440196

20020404 <--

AU 2002338309 A1 20021021 AU 2002-338309

20020404 <--

EP 1379269 A1 20040114 EP 2002-759761

20020404 <--

EP 1379269 B1 20090304

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,

IE, SI, LT, LV, FI, RO, MK, CY, AL, TR

JP 2004529916 T 20040930 JP 2002-578996

20020404 <--

US 20040097540 A1 20040520 US 2003-473809

20031002 <--

US 7160899 B2 20070109

MX 2003009185 A 20040217 MX 2003-9185

20031008 <--

PRAI DK 2001-583 A 20010409 <--

WO 2002-DK228 W 20020404 <--

IT Nerve

(dopaminergic; adenosine A2A receptor antagonists combined with neurotrophic compds. in treatment of Parkinson's disease)

IT Brain  
(nigrostriatal dopaminergic tract; adenosine A2A receptor antagonists combined with neurotrophic compds. in treatment of Parkinson's disease)

IT 51-61-6, Dopamine, biological studies  
RL: BSU (Biological study, unclassified); BIOL (Biological study)  
(adenosine A2A receptor antagonists combined with neurotrophic compds.  
in treatment of Parkinson's disease)

IT 14114-46-6, DMPX 104615-18-1, CGS-15943 139180-30-6, ZM-241385  
141807-96-7, KF-17837 155270-99-8, KW-6002 160098-96-4,  
SCH-58261 160753-58-2 309711-72-6  
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL  
(Biological study); USES (Uses)  
(adenosine A2A receptor antagonists combined with neurotrophic compds.  
in treatment of Parkinson's disease)

L20 ANSWER 3 OF 6 CAPLUS COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 2002:943 CAPLUS Full-text

DOCUMENT NUMBER: 137:88308

TITLE: Adenosine A2A receptor antagonists: Potential therapeutic and neuroprotective effects in

Parkinson's

disease

AUTHOR(S): Morelli, M.; Wardas, J.

CORPORATE SOURCE: Department of Toxicology, University of Cagliari,

Palazzo delle Scienze, Cagliari, 09124, Italy

SOURCE: Neurotoxicity Research (2001), 3(6), 545-556

CODEN: NURRFI; ISSN: 1029-8428

PUBLISHER: Harwood Academic Publishers

DOCUMENT TYPE: Journal

LANGUAGE: English

AB The most effective treatment of Parkinson's disease (PD) is, at present, the dopamine precursor L-3,4-dihydroxyphenyl-alanine (L-DOPA), however a number of disadvantages such as a loss of drug efficacy and severe side-effects (psychoses, dyskinesias and on-off phenomena) limit long-term, effective utilization of this drug. Recent exptl. studies in which selective antagonists of adenosine A2A receptors were used, have shown an improvement in motor disabilities in animal models of PD. The A2A antagonist [7-(2-phenylethyl)-5-amino-2-(2-furyl)-pyrazolo- (4,3-e)-1,2,4-triazolo(1,5--c)pyrimidine] (SCH 58261) potentiated the contralateral turning behavior induced by a threshold dose of L-DOPA or direct dopamine receptor agonists in unilaterally 6-hydroxydopamine (6-OHDA) lesioned rats, an effect accompanied by an increase in Foslike-immunoreactivity in neurons of the lesioned striatum. Likewise, other A2A receptor antagonists such as (3,7-dimethyl-1-propargylxanthine) (DMPX), [E-8-(3,4-dimethoxystyryl)-1,3-dipropyl-7-methylxanthine] (KF 17837) and [E-1,3-diethyl-8-(3,4-dimethoxystyryl)-7-methyl-3,7-dihydro-1H-purine-2, 6-dione] (KW 6002) antagonized catalepsy induced by haloperidol or reserpine in the rat, whereas in non-human primate models of PD, KW 6002 reduced the rigidity and improved the disability score of

MPTP-treated marmosets and cynomolgus monkeys. Moreover, in contrast to L-DOPA, selective A2A receptor antagonists administered chronically did not produce dyskinesias and did not evoke tolerance in 6-OHDA and MPTP models of PD. An addnl. therapeutic potential of adenosine A2A antagonists emerged from studies showing neuroprotective properties of these compds. in animal models of cerebral ischemia and excitotoxicity, as well as in the (1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine) (MPTP) model of PD. Adenosine A2A receptor antagonists by reversing motor impairments in animal models of PD and by contrasting cell degeneration are some of the most promising compds. for the treatment of PD.

TI Adenosine A2A receptor antagonists: Potential therapeutic and neuroprotective effects in Parkinson's disease

REFERENCE COUNT: 87 THERE ARE 87 CITED REFERENCES AVAILABLE FOR THIS

RECORD. ALL CITATIONS AVAILABLE IN THE

RE FORMAT

SO Neurotoxicity Research (2001), 3(6), 545-556  
CODEN: NURRFI; ISSN: 1029-8428

L20 ANSWER 4 OF 6 CAPLUS COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 2000:828333 CAPLUS Full-text

DOCUMENT NUMBER: 134:157476

TITLE: Adenosine A2A receptor antagonists KF17837 and KW-6002

potentiate rotation induced by dopaminergic drugs in hemi-Parkinsonian rats

AUTHOR(S): Koga, K.; Kurokawa, M.; Ochi, M.; Nakamura, J.;

Kuwana, Y.

CORPORATE SOURCE: Pharmaceutical Research Institute, Kyowa Hakko Kogyo

Co. Ltd., Shizuoka, Sunto-gun, Nagaizumi-cho, 411-8731, Japan

SOURCE: European Journal of Pharmacology (2000), 408(3), 249-255

CODEN: EJPHAZ; ISSN: 0014-2999

PUBLISHER: Elsevier Science B.V.

DOCUMENT TYPE: Journal

LANGUAGE: English

AB The effects of novel adenosine A2A receptor antagonists KF17837 ((E)-1,3-dipropyl-8-(3,4-dimethoxystyryl)-7-methyl-3,7-dihydro-1H-purine-2,6-dione) and KW-6002 ((E)-1,3-diethyl-8-(3,4-dimethoxystyryl)-7-methyl-3,7-dihydro-1H-purine-2,6-dione), on rotational behavior induced by apomorphine or L-DOPA (1-3,4-dihydroxyphenylalanine) were investigated in rats with unilateral 6-hydroxydopamine lesions. Both KF17837 and KW-6002 slightly induced rotational behavior per se. However, KF17837 and KW-6002 significantly increased the total counts of turning induced by apomorphine at doses of 3 mg/kg, p.o. and 10 mg/kg, p.o., and at doses of 1 mg/kg, p.o. and higher, resp. KF17837 and KW-6002 also potentiated the rotational behavior induced by L-DOPA at a dose of 3 mg/kg, p.o. Furthermore, i.c.v. injection (10 µg/20 µl) of a selective adenosine A2 receptor agonist CGS 21680 {2-[p-(2-carboxyethyl)phenethylamino]-5'-N-ethylcarboxamidoadenosine}

partially prevented the rotational behavior induced by apomorphine and this inhibition was reversed by KW-6002 (1 mg/kg, p.o.). The increase in total counts of apomorphine-induced turning by the adenosine A2A receptor antagonists seems to be mainly attributable to prolongation of turning duration rather than enhancement of intensity. These results suggest that these adenosine A2A receptor antagonists may be useful to ameliorate shortening in the duration of dopaminergic drug response in patients with advanced Parkinson's disease.

TI Adenosine A2A receptor antagonists KF17837 and KW-6002 potentiate rotation

induced by dopaminergic drugs in hemi-Parkinsonian rats

REFERENCE COUNT: 26 THERE ARE 26 CITED REFERENCES AVAILABLE FOR THIS

RECORD. ALL CITATIONS AVAILABLE IN THE

RE FORMAT

TI Adenosine A2A receptor antagonists KF17837 and KW-6002 potentiate rotation

induced by dopaminergic drugs in hemi-Parkinsonian rats

L20 ANSWER 5 OF 6 CAPLUS COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 1998:394679 CAPLUS Full-text

DOCUMENT NUMBER: 129:118143

ORIGINAL REFERENCE NO.: 129:24113a,24116a

TITLE: Pharmacological characterization of a simple behavioral response mediated selectively by

central

adenosine A1 receptors, using in vivo and in

vitro

techniques

AUTHOR(S):

Marston, Hugh M.; Finlayson, Keith; Maemoto,

Takuya;

Olverman, Henry J.; Akahane, Atsushi; Sharkey,

John;

Butcher, Steven P.

CORPORATE SOURCE:

Fujisawa Institute of Neuroscience, University

of

Edinburgh, Edinburgh, UK

SOURCE:

Journal of Pharmacology and Experimental

Therapeutics

(1998), 285(3), 1023-1030

CODEN: JPETAB; ISSN: 0022-3565

PUBLISHER:

Williams & Wilkins

DOCUMENT TYPE:

Journal

LANGUAGE:

English

AB The behavioral profile of a range of adenosine receptor ligands was examined in rats using a locomotor activity model. Adenosine receptor agonists, including the selective A1 receptor agonist, N6-cyclopentyladenosine (CPA) and the A2A agonist, 2-[(2-aminoethylamino)carbonylethyl-phenylethylamino]- 5'-ethylcarboxamidoadenosine (APEC), reduced spontaneous motor activity in a dose-dependent manner. CPA-induced locomotor depression was attenuated by adenosine A1 receptor selective antagonists, such as 8-cyclopentyl-1,3-dipropylxanthine (DPCPX), (R)-1-[(E)-3-(2-phenylpyrazolo[1,5-a]pyridin-3-yl)-acryloyl]-2-piperidine ethanol (FK453), and (R)-1-[(E)-3-(2-

phenylpyrazolo[1,5-a]pyridin-3-yl)-acryloyl]-piperidin-2-yl acetic acid (FK352), but not by the A2A receptor antagonist, (E)-1,3-dipropyl-8-(3,4-dimethoxystyryl)-7-methylxanthine (KF17837). By contrast, APEC-induced hypolocomotion was attenuated by KF17837 but not by DPCPX, confirming that adenosine A1 and A2A receptor activation mediates locomotor output independently. Two peripheral adenosine receptor antagonists, 8-(p-sulfophenyl)-1,3-dipropylxanthine (DPSPX) and 8-(p-sulfophenyl)-1,3-dimethylxanthine (8-PST), did not alter CPA-induced hypolocomotion. This confirmed that pharmacol. reversal of the adenosine A1 receptor-mediated response involved a central site of drug action. The relationship between occupancy of central adenosine A1 receptors and behavioral effect was therefore assessed. Regression anal. on log transformed data confirmed assocns. between antagonist affinity for brain [3H]DPCPX binding sites and, in order of increasing significance, the equivalent behavioral dose (EBD) for reversal of CPA-induced hypolocomotion ( $R^2 = 0.32$ ), the serum concentration of drug ( $R^2 = 0.65$ ), and most significantly with the brain concentration of drug detected 20 min after administration of the (EBD) ( $R^2 = 0.95$ ). These data suggest that competition between agonists and antagonists, for occupancy of central adenosine A1 receptors, is intrinsic to the pharmacol. reversal of CPA-induced hypolocomotion. The validity of the model as a simple predictive screen for the blood/brain barrier permeability of adenosine A1 receptor antagonists was thereby confirmed.

L20 ANSWER 6 OF 6 CAPLUS COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 1994:315658 CAPLUS [Full-text](#)

DOCUMENT NUMBER: 120:315658

ORIGINAL REFERENCE NO.: 120:55249a,55252a

TITLE: KF17837: a novel selective adenosine A2A receptor

antagonist with anticataleptic activity  
AUTHOR(S): Kanda, Tomoyuki; Shiozaki, Shizuo; Shimada, Junichi;

Suzuki, Fumio; Nakamura, Joji  
CORPORATE SOURCE: Pharmaceutical Research Laboratories, Kyowa Hakko  
Kogyo Co. Ltd., 1188 Shimotogari, Nagaizumi-Cho,

Sunto-Gun, Shizuoka, 411, Japan  
SOURCE: European Journal of Pharmacology (1994), 256(3), 263-8  
CODEN: EJPHAZ; ISSN: 0014-2999

DOCUMENT TYPE: Journal

LANGUAGE: English

AB KF17837 is a novel selective adenosine A2A receptor antagonist. Oral administration of KF17837 (2.5, 10.0 and 30.0 mg/kg) significantly ameliorated the cataleptic responses induced by intracerebroventricular administration of an adenosine A2A receptor agonist, CGS 21680 (10  $\mu$ g), in a dose-dependent manner. KF17837 also reduced the catalepsy induced by haloperidol (1 mg/kg i.p.) and by reserpine (5 mg/kg i.p.). These anticataleptic effects were exhibited dose dependently at doses from 0.625 and 2.5 mg/kg p.o., resp. Moreover, KF17837 (0.625 mg/kg p.o.) potentiated the anticataleptic effects of a subthreshold dose of L-3,4-dihydroxyphenylalanine (L-DOPA; 25 mg/kg i.p.) plus

benserazide (6.25 mg/kg i.p.). These results suggested that KF17837 is a centrally active adenosine A2A receptor antagonist and that the dopaminergic function of the nigrostriatal pathway is potentiated by adenosine A2A receptor antagonists. Furthermore, KF17837 may be a useful drug in the treatment of parkinsonism.

TI KF17837: a novel selective adenosine A2A receptor antagonist with anticataleptic activity

=> s l14 and (py<2003 or ay<2003 or pry<2003)

22983605 PY<2003

4504987 AY<2003

3974028 PRY<2003

L21 43 L14 AND (PY<2003 OR AY<2003 OR PRY<2003)

=> d l21 ibib abs ti hit 33-43

L21 ANSWER 33 OF 43 CAPLUS COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 1994:483358 CAPLUS Full-text

DOCUMENT NUMBER: 121:83358

ORIGINAL REFERENCE NO.: 121:14985a,14988a

TITLE: preparation of xanthine derivatives as

antidepressants

INVENTOR(S): Suzuki, Fumio; Shimada, Junichi; Ishii, Akio; Nakamura, Joji; Ichikawa, Shunji; Kitamura,

Shigeto;

Koike, Nobuaki

PATENT ASSIGNEE(S): Kyowa Hakko Kogyo Co., Ltd., Japan

SOURCE: PCT Int. Appl., 173 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

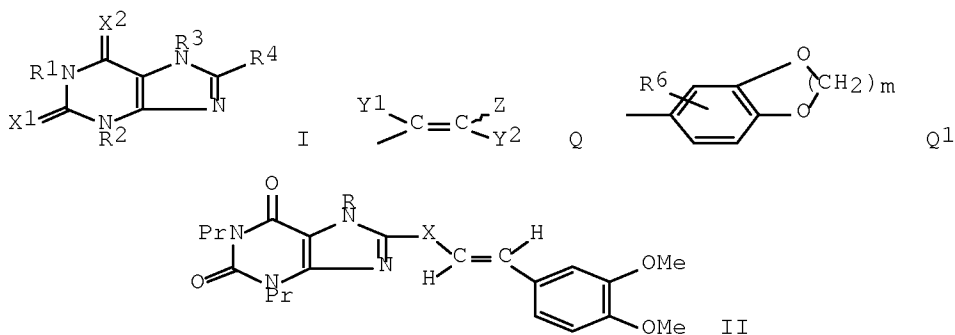
LANGUAGE: Japanese

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
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WO 9401114	A1	19940120	WO 1993-JP931	
19930707 <--				
W: CA, JP, NO, US				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL,				
PT, SE				
EP 628311	A1	19941214	EP 1993-914963	
19930707 <--				
EP 628311	B1	20020424		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC,				
NL, PT, SE				
JP 2928386	B2	19990803	JP 1993-502746	
19930707 <--				
AT 216584	T	20020515	AT 1993-914963	
19930707 <--				
PT 628311	T	20020930	PT 1993-914963	
19930707 <--				
ES 2176204	T3	20021201	ES 1993-914963	
19930707 <--				
CA 2116967	C	20030819	CA 1993-2116967	

19930707 <--  
 US 5543415 A 19960806 US 1994-199142  
 19940225 <--  
 NO 9400737 A 19940503 NO 1994-737  
 19940303 <--  
 PRIORITY APPLN. INFO.: JP 1992-181025 A  
 19920708 <--  
 WO 1993-JP931 W  
 19930707 <--  
 OTHER SOURCE(S): MARPAT 121:83358  
 GI



AB Xanthine derivs. [I; R1, R2, R3 = H, alkyl, allyl, propargyl; R4 = cycloalkyl, -(CH2)nR5 (wherein R5 = optionally substituted aryl, heterocyclic group, and n = 0-4), Q (wherein Y1, Y2 = H, F, Me; Z = optionally substituted aryl, Q1 wherein R6 = H, OH, alkyl, alkoxy, halo, nitro or amino; m = 1-3), optionally substituted heterocyclic group; X1, X2 = O or S] are prepared A mixture of 5,6-diamino-1,3-dipropyluracil, 3,4-dimethoxycinnamic acid, and 3-(3-diethylaminopropyl)-1- ethylcarbodiimide HCl in dioxane-H2O was stirred at room temperature and pH 5.5 to give 94% amide II (R = H, X = NHCO), which was refluxed with 1N NaOH in dioxane to give 77% styryl compound II (R = H, X = bond) (III). Methylation of III with MeI and K2CO3 in DMF at 50° gave 98% Me derivative II (R = Me, X = bond), which at 2.5 mg/kg p.o. in mice showed 4.8-fold increase in clonidine-induced aggression, vs. control.

TI preparation of xanthine derivatives as antidepressants

REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS

RECORD. ALL CITATIONS AVAILABLE IN THE

RE FORMAT

PI	WO 9401114 A1	19940120			
	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
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PI	WO 9401114	A1	19940120	WO 1993-JP931	

19930707 <--

W: CA, JP, NO, US

RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL,

PT, SE

EP 628311	A1	19941214	EP 1993-914963
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EP 628311	B1	20020424	
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE			
JP 2928386	B2	19990803	JP 1993-502746
19930707 <--			
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19930707 <--			
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ES 2176204	T3	20021201	ES 1993-914963
19930707 <--			
CA 2116967	C	20030819	CA 1993-2116967
19930707 <--			
US 5543415	A	19960806	US 1994-199142
19940225 <--			
NO 9400737	A	19940503	NO 1994-737
19940303 <--			
PRAI JP 1992-181025	A	19920708	<--
WO 1993-JP931	W	19930707	<--

L21 ANSWER 34 OF 43 CAPLUS COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 1994:473411 CAPLUS [Full-text](#)

DOCUMENT NUMBER: 121:73411

ORIGINAL REFERENCE NO.: 121:12911a,12914a

TITLE: Effects of the new A2 adenosine receptor antagonist

8FB-PTP, an 8 substituted  
pyrazolo-triazolo-pyrimidine, on in vitro  
functional

models

AUTHOR(S): Dionisotti, Silvio; Conti, Annamaria; Sandoli, Daniele; Zocchi, Cristina; Gatta, Franco; Ongini,

Ennio

CORPORATE SOURCE: Res. Lab., Schering-Plough S.p.A., Comazzo, 20060,

Italy

SOURCE: British Journal of Pharmacology (1994), 112(2), 659-65

CODEN: BJPCBM; ISSN: 0007-1188

DOCUMENT TYPE: Journal

LANGUAGE: English

AB The authors have characterized the in vitro pharmacol. profile of putative A2 adenosine antagonists, two non-xanthine compds., 5-amino-8-(4-fluorobenzyl)-2-(2-furyl)-pyrazolo [4,3-e]-1,2,4-triazolo[1,5-c]pyrimidine (8FB-PTP) and 5-amino-9-chloro-2-(2-furyl)-1,2,4-triazolo[1,5-c]quinazoline (CGS 15943), and the xanthine derivative (E)7-methyl-8-(3,4-dimethoxystyryl)-1,3-dipropyl-xanthine (KF 17837). In binding studies on bovine brain, 8FB-PTP was the most potent (K<sub>i</sub> = 0.074 nM) and selective (28 fold) drug on A2 receptors, whereas CGS 15943 and KF 17837 exhibited affinity in the low and high nanomolar range, resp., and showed little selectivity. In functional studies, 8FB-PTP antagonized 5'-N-ethylcarboxamidoadenosine (NECA)-induced

vasorelaxation of bovine coronary artery ( $pA_2 = 7.98$ ) and NECA-induced inhibition of rabbit platelet aggregation ( $pA_2 = 8.20$ ). CGS 15943 showed weak activity in the platelet aggregation model ( $pA_2 = 7.43$ ) and failed to antagonized NECA-induced vasodilation. KF 17837 was ineffective in both models up to micromolar concns. Antagonism of A<sub>1</sub>-mediated responses was tested vs. 2-chloro-N<sup>6</sup>-cyclopentyladenosine (CCPA) in rat atria. 8FB-PTP and CGS 15943 also antagonized competitively the neg. chronotropic response induced by CCPA. Conversely, KF 17837 was unable to reverse A<sub>1</sub>-mediated responses. 8FB-PTP is a potent and competitive antagonist of responses mediated by A<sub>2</sub> adenosine receptors. The data provided a basis to reduce, by further chemical modifications, the affinity at A<sub>1</sub> receptor and therefore enhance A<sub>2</sub> receptor selectivity.

TI Effects of the new A<sub>2</sub> adenosine receptor antagonist 8FB-PTP, an 8 substituted pyrazolo-triazolo-pyrimidine, on in vitro functional models

SO British Journal of Pharmacology (1994), 112(2), 659-65  
CODEN: BJPCBM; ISSN: 0007-1188

IT 104615-18-1, CGS 15943 141807-96-7, KF 17837 154910-02-8  
RL: BIOL (Biological study)  
(pharmacol. profile of, as A<sub>2</sub> adenosine receptor antagonist)

L21 ANSWER 35 OF 43 CAPLUS COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 1994:426752 CAPLUS Full-text

DOCUMENT NUMBER: 121:26752

ORIGINAL REFERENCE NO.: 121:4705a, 4708a

TITLE: KF17837 ((E)-8-(3,4-dimethoxystyryl)-1,3-dipropyl-7-

adenosine A<sub>2</sub>

receptor antagonist  
AUTHOR(S): Nonaka, Hiromi; Ichimura, Michio; Takeda, Masami;  
Nonaka, Yoshiko; Shimada, Jyunichi; Suzuki, Fumio;

Yamaguchi, Kazuo; Kase, Hiroshi  
CORPORATE SOURCE: Pharmaceutical Research Laboratories, Kyowa

Hakko  
Kogyo Co., Ltd., 1188 Shimotogari, Sunto,

Shizuoka,  
411, Japan

SOURCE: European Journal of Pharmacology, Molecular Pharmacology Section (1994), 267(3), 335-41  
CODEN: EJPPET; ISSN: 0922-4106

DOCUMENT TYPE: Journal

LANGUAGE: English

AB 8-(3,4-Dimethoxystyryl)-1,3-dipropyl-7-methylxanthine exhibited high affinity and selectivity for adenosine A<sub>2A</sub> receptors in binding assay using rat striatal A<sub>2A</sub> receptors labeled with [3H]2-[p-(2-carboxyethyl)-phenethylamino]-5'-N-ethylcarboxamidoadenosine (CGS21680). The affinity was stereo selective: the E isomer, KF17837, showed a K<sub>i</sub> value of 1.0±0.057 nM for the A<sub>2A</sub> receptors, whereas the Z isomer showed much lower affinity. KF17837 had 62-fold selectivity for the A<sub>2A</sub> receptors vs. rat forebrain A<sub>1</sub> receptors labeled with [3H]N<sup>6</sup>-cyclohexyladenosine (CHA). KF17837 was rapidly photoisomerized to form a stable equilibrium mixture

(18% E - 82% Z), KF17837S, which showed  $K_i$  values of  $7.9 \pm 0.055$  nM and  $390 \pm 68$  nM for the A2A and A1 receptors, resp. The inhibition type was competitive for [3H]CGS21680 binding. In rat pheochromocytoma PC12 cells KF17837S antagonized cAMP accumulation induced by 1  $\mu$ M CGS21680 via the A2A receptors, with an  $IC_{50}$  value of  $53 \pm 10$  nM. cAMP accumulation induced by 10  $\mu$ M 5'-N-ethylcarboxamidoadenosine via the A2B receptors in Jurkat cells (human T-cell line) was inhibited by KF17837S with an  $IC_{50}$  value of  $1500 \pm 290$  nM. These results indicate that KF17837S (and hence KF17837) is a highly potent and selective adenosine A2A receptor antagonist.

TI KF17837 ((E)-8-(3,4-dimethoxystyryl)-1,3-dipropyl-7-methylxanthine), a  
potent and selective adenosine A2 receptor antagonist  
SO European Journal of Pharmacology, Molecular Pharmacology Section (1994), 267(3), 335-41  
CODEN: EJPPET; ISSN: 0922-4106  
IT 141867-96-7, KF17837 149744-74-1, KF 17837S  
RL: BIOL (Biological study)  
(as potent and selective adenosine A2A receptor antagonist)

L21 ANSWER 36 OF 43 CAPLUS COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 1994:315658 CAPLUS Full-text  
DOCUMENT NUMBER: 120:315658  
ORIGINAL REFERENCE NO.: 120:55249a,55252a  
TITLE: KF17837: a novel selective adenosine A2A  
receptor

antagonist with anticataleptic activity  
AUTHOR(S): Kanda, Tomoyuki; Shiozaki, Shizuo; Shimada,  
Junichi;  
Suzuki, Fumio; Nakamura, Joji  
CORPORATE SOURCE: Pharmaceutical Research Laboratories, Kyowa  
Hakko  
Kogyo Co. Ltd., 1188 Shimotogari, Nagaizumi-

Cho,  
Sunto-Gun, Shizuoka, 411, Japan  
SOURCE: European Journal of Pharmacology (1994),  
256(3), 263-8  
CODEN: EJPHAZ; ISSN: 0014-2999

DOCUMENT TYPE: Journal  
LANGUAGE: English

AB KF17837 is a novel selective adenosine A2A receptor antagonist.  
Oral administration of KF17837 (2.5, 10.0 and 30.0 mg/kg)  
significantly ameliorated the cataleptic responses induced by  
intracerebroventricular administration of an adenosine A2A  
receptor agonist, CGS 21680 (10  $\mu$ g), in a dose-dependent manner.  
KF17837 also reduced the catalepsy induced by haloperidol (1 mg/kg  
i.p.) and by reserpine (5 mg/kg i.p.). These anticataleptic  
effects were exhibited dose dependently at doses from 0.625 and  
2.5 mg/kg p.o., resp. Moreover, KF17837 (0.625 mg/kg p.o.)  
potentiated the anticataleptic effects of a subthreshold dose of  
L-3,4-dihydroxyphenylalanine (L-DOPA; 25 mg/kg i.p.) plus  
benserazide (6.25 mg/kg i.p.). These results suggested that  
KF17837 is a centrally active adenosine A2A receptor antagonist  
and that the dopaminergic function of the nigrostriatal pathway is

potentiated by adenosine A2A receptor antagonists. Furthermore, KF17837 may be a useful drug in the treatment of parkinsonism.

TI KF17837: a novel selective adenosine A2A receptor antagonist with anticataleptic activity

SO European Journal of Pharmacology (1994), 256(3), 263-8  
CODEN: EJPHAZ; ISSN: 0014-2999

IT 141807-96-7, KF17837  
RL: BIOL (Biological study)  
(adenosine A2A receptor antagonist, dopaminergic function potentiation  
by, anticataleptic effects in relation to)

L21 ANSWER 37 OF 43 CAPLUS COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 1994:236103 CAPLUS Full-text

DOCUMENT NUMBER: 120:236103

ORIGINAL REFERENCE NO.: 120:41569a, 41572a

TITLE: KF17837 is an A2 adenosine receptor antagonist in vivo

AUTHOR(S): Jackson, Edwin K.; Herzer, William A.; Suzuki, Fumio

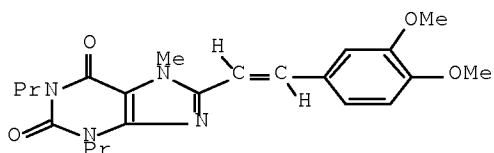
CORPORATE SOURCE: Med. Cent., Univ. Pittsburgh, Pittsburgh, PA, USA

SOURCE: Journal of Pharmacology and Experimental Therapeutics  
(1993), 267(3), 1304-10  
CODEN: JPETAB; ISSN: 0022-3565

DOCUMENT TYPE: Journal

LANGUAGE: English

GI



AB The goal of this study was to determine whether KF17837 (I) is a useful pharmacol. probe for investigating in the rat the in vivo physiol. roles of A2 adenosine receptors. In anesthetized rats, bradycardic responses to N6-cyclopentyladenosine and hypotensive responses to 2-[p-(2-carboxyethyl)phenethylamino]-5'-N-ethylcarboxamido adenosine (CGS21680C) were used to assess A1 receptor and A2 receptor activation, resp. After obtaining control responses to N6-cyclopentyladenosine and CGS21680C, the rats received infusions of either vehicle or one of two dosage levels of KF17837, a compound recently demonstrated to be a potent and selective A2 receptor antagonist in vitro. KF17837 was infused for 4 h and, at various times during the infusions, bradycardic and hypotensive responses to N6-cyclopentyladenosine and CGS21680C, resp., were elicited. Infusion of either 10 or 30 µg kg<sup>-1</sup> min<sup>-1</sup> (2.4 or 7.4 mg kg<sup>-1</sup> 4 h<sup>-1</sup>) of KF17837 did not significantly affect the bradycardic responses to N6-

cyclopentyladenosine. By contrast, 10 µg kg<sup>-1</sup> min<sup>-1</sup> of KF17837 attenuated and 30 µg kg<sup>-1</sup> min<sup>-1</sup> of KF17837 nearly abolished hypotensive responses to CGS21680C. In a second study, pretreatment with KF17837 (30 µg kg<sup>-1</sup> min<sup>-1</sup>) did not affect the hypotensive response to either PGI<sub>2</sub> (3 µg kg<sup>-1</sup> min<sup>-1</sup>) or acetylcholine (100 µg kg<sup>-1</sup> min<sup>-1</sup>); however, it attenuated the hypotensive response to adenosine (300 µg kg<sup>-1</sup> min<sup>-1</sup>). In a third study, hypotension was induced and maintained with an infusion of adenosine (300 µg kg<sup>-1</sup> min<sup>-1</sup>). Subsequent initiation of an infusion of KF17837 (30 µg kg<sup>-1</sup> min<sup>-1</sup>) completely reversed the adenosine-induced hypotension. This study suggests that in vivo KF17837 has relative selectivity for the A<sub>2</sub> receptor and may be a useful pharmacol. probe for elucidating the role of endogenous adenosine-A<sub>2</sub> receptor interactions in vivo in the rat.

TI KF17837 is an A<sub>2</sub> adenosine receptor antagonist in vivo  
 SO Journal of Pharmacology and Experimental Therapeutics (1993),  
 267(3), 1304-10

CODEN: JPETAB; ISSN: 0022-3565

IT 141807-96-7, KF 17837

RL: BIOL (Biological study)

(A<sub>2</sub> adenosine receptor antagonism by, specificity of)

L21 ANSWER 38 OF 43 CAPLUS COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 1994:144161 CAPLUS Full-text

DOCUMENT NUMBER: 120:144161

ORIGINAL REFERENCE NO.: 120:25227a,25230a

TITLE: Pharmaceutical compositions containing  
 xanthine

derivatives for treatment of Parkinson's

disease

INVENTOR(S): Suzuki, Fumio; Shimada, Junichi; Ishii, Akio;  
 Ichikawa, Shunji

PATENT ASSIGNEE(S): Kyowa Hakko Kogyo Co., Ltd., Japan

SOURCE: Eur. Pat. Appl., 49 pp.

CODEN: EPXXDW

DOCUMENT TYPE: Patent

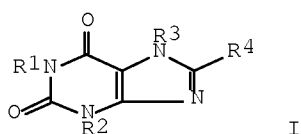
LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
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EP 565377	A1	19931013	EP 1993-302780	
19930408 <--				
EP 565377	B1	19980107		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC,				
NL, PT, SE				
CA 2093403	A1	19931009	CA 1993-2093403	
19930405 <--				
CA 2093403	C	19990810		
NO 9301317	A	19931011	NO 1993-1317	
19930406 <--				
NO 303265	B1	19980622		
JP 06016559	A	19940125	JP 1993-81953	

19930408 <--  
 JP 2613352 B2 19970528  
 AT 161723 T 19980115 AT 1993-302780  
 19930408 <--  
 ES 2112386 T3 19980401 ES 1993-302780  
 19930408 <--  
 PRIORITY APPLN. INFO.: JP 1992-87115 A  
 19920408 <--  
 OTHER SOURCE(S): MARPAT 120:144161  
 GI



AB Pharmaceutical compns. containing xanthine derivs. (I; R1, R2, R3=H, C1-6 alkyl or allyl; R4= C3-8 cycloalkyl) are useful for treatment of Parkinson's disease. (E)-6-amino-5-(3,4-dimethoxycinnamoyl)amino-1,3- dipropyluracil (preparation is given) was refluxed in NaOH solution, then was neutralized and the deposited crysts. were separated to to obtain (E)-8-(3,4-dimethoxystyryl)-1,3-dipropylxanthine (II). To II in DMF was added K2CO3 and MeI and the mixture was heated at 50° for 30min followed by filtration and addition of water. The filtrate was extracted with CHCl3 and the extract was washed, dried, evaporated, and purified to obtain (E)-8-(3,4-dimethoxystyryl)-7-methyl-1,3-dipropylxanthine (III). A tablet contained III 20, lactose 143.4, potato starch 30, hydroxypropyl cellulose 6, and Mg stearate 0.6mg.

TI Pharmaceutical compositions containing xanthine derivatives for treatment

of Parkinson's disease

PI EP 565377 A1 19931013

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
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PI EP 565377	A1	19931013	EP 1993-302780	
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19930408 <--

EP 565377	B1	19980107		
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R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC,

NL, PT, SE

CA 2093403	A1	19931009	CA 1993-2093403	
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19930405 <--

CA 2093403	C	19990810		
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NO 9301317	A	19931011	NO 1993-1317	
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NO 303265	B1	19980622		
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JP 06016559	A	19940125	JP 1993-81953	
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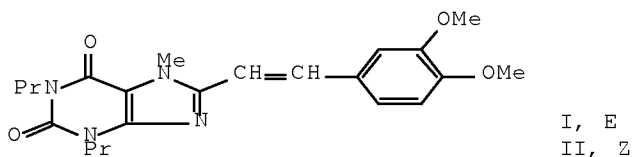
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JP 2613352	B2	19970528		
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AT 161723	T	19980115	AT 1993-302780
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ES 2112386	T3	19980401	ES 1993-302780
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PRAI JP 1992-87115	A	19920408 <--	
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RL: PREP (Preparation)  
(preparation of, pharmaceutical composition containing, for  
treatment of Parkinson's  
disease)

L21 ANSWER 39 OF 43 CAPLUS COPYRIGHT 2009 ACS on STN  
ACCESSION NUMBER: 1994:124633 CAPLUS Full-text  
DOCUMENT NUMBER: 120:124633  
ORIGINAL REFERENCE NO.: 120:21765a,21768a  
TITLE: Photoisomerization of a potent and selective  
adenosine  
A2 antagonist,  
(E)-1,3-dipropyl-8-(3,4-dimethoxystyryl)-7-  
methylxanthine  
AUTHOR(S): Nonaka, Yoshiko; Shimada, Junichi; Nonaka,  
Hiromi;  
Koike, Nobuaki; Aoki, Noboru; Kobayashi,  
Hiroyuki;  
Kase, Hiroshi; Yamaguchi, Kazuo; Suzuki, Fumio  
CORPORATE SOURCE: Pharm. Res. Lab., Kyowa Hakko Kogyo Co., Ltd.,  
Nagaizumi, 411, Japan  
SOURCE: Journal of Medicinal Chemistry (1993),  
36(23), 3731-3  
CODEN: JMCMAR; ISSN: 0022-2623  
DOCUMENT TYPE: Journal  
LANGUAGE: English  
GI



AB 1,3,7-Trialkylxanthines with (E)-8-styryl substituents are selective adenosine A2 receptor antagonists. The photoisomerization and binding affinity of (E)- (I) and (Z)-1,3-dipropyl-8-(3,4-dimethoxystyryl)-7-methylxanthines (II) have been examined. Compound I was isomerized to its Z-isomer II under photo illumination by fluorescent light (1000 lx) in DMSO or methanol. Its photoisomerization was slow at high concentration (10 mM) of substrate but was fast at low concentration (0.1 mM) and an equilibrium mixture (82% Z-18%E) was eventually formed. This finding was substantiated by similarly exposing the Z-isomer II (0.1 mM) and obtaining the same equilibrium mixture. The E-isomer I possesses potent affinity ( $K_i = 1.0$  nM,  $K_i$  ratio of A1/A2 = 62) at the A2 receptor that is 800-fold higher than its Z-isomer II. Then the authors examined possibility of the E-Z isomerization in animals. Plasma and brain concns. of I 4 h after its oral administration in rats at a dose of 30 mg/kg, were 0.065  $\mu\text{g/mL}$  and 0.076  $\mu\text{g/g}$  brain, resp. None of the Z-isomer II was detected in plasma and brain. Although these concns. of I indicate poor oral bioavailability, they are sufficient to fully antagonize adenosine receptors in the heart and the CNS. Thus, compound I might be a useful pharmacol. probe in vivo for elucidating the physiol. and pathophysiol. roles of the A2 receptor.

TI Photoisomerization of a potent and selective adenosine A2 antagonist,

(E)-1,3-dipropyl-8-(3,4-dimethoxystyryl)-7-methylxanthine

SO Journal of Medicinal Chemistry (1993), 36(23), 3731-3

CODEN: JMCMAR; ISSN: 0022-2623

IT 141807-96-7

RL: BIOL (Biological study)

(adenosinergic A2 antagonist activity and photoisomerization of)

L21 ANSWER 40 OF 43 CAPLUS COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 1993:254617 CAPLUS [Full-text](#)

DOCUMENT NUMBER: 118:254617

ORIGINAL REFERENCE NO.: 118:44233a,44236a

TITLE: Structure-activity relationships of 8-styrylxanthines

as A2-selective adenosine antagonists

AUTHOR(S): Jacobson, Kenneth A.; Gallo-Rodriguez, Carola; Melman,

Neli; Fischer, Bilha; Maillard, Michel; van

Bergen,

Andrew; van Galen, Philip J. M.; Karton,

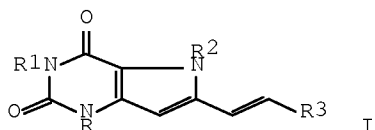
Yishai

CORPORATE SOURCE: Lab. Bioorg. Chem., Natl. Inst. Diabet.,

Digest.

SOURCE: Kidney Dis., Bethesda, MD, 20892, USA  
Journal of Medicinal Chemistry (1993),  
36(10), 1333-42  
CODEN: JMCMAR; ISSN: 0022-2623

DOCUMENT TYPE: Journal  
LANGUAGE: English  
GI



AB A series of substituted 8-styryl derivs. of 1,3,7-alkylxanthines I [i.e., R-R2 = H, Me, R3 = (un)substituted Ph] was synthesized as potential A2-selective adenosine receptor antagonists, and the potency at rat brain A1- and A2-receptors was studied in radioligand binding expts. At the xanthine 7-position, only small hydrophobic substituents were tolerated in receptor binding. 7-Me analogs were roughly 1 order of magnitude more selective for A2 vs. A1 receptors than the corresponding 7-H analogs. 1,3-Dimethylxanthine derivs. tended to be more selective for A2-receptors than the corresponding 1,3-diallyl, di-Et, or di-Pr derivs. Substitutions of the Ph ring at the 3-(monosubstituted) and 3,5-(disubstituted) positions were favored. I (R - R2 = Me, R3 = 3-ClC6H4) was a moderately potent and high A2-selective adenosine antagonist. I (R - R2 = Me, R3 = 3-HO2CCH2CH2CONHC6H4) was highly A2-selective and had enhanced water solubility I [R, R1 = Pr, R2 = Me, R3 = 3,5-(MeO)2C6H3] was a potent and very A2-selective adenosine antagonist.

TI Structure-activity relationships of 8-styrylxanthines as A2-selective adenosine antagonists

SO Journal of Medicinal Chemistry (1993), 36(10), 1333-42  
CODEN: JMCMAR; ISSN: 0022-2623

IT 51389-37-8P 99765-13-6P 132940-42-2P 141807-95-6P  
141807-96-7P 142665-36-9P 147699-92-1P 147699-93-2P  
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 147700-54-7P 147700-55-8P

RL: SPN (Synthetic preparation); PREP (Preparation)  
 (preparation and A2-selective adenosine antagonistic activity  
 of)

L21 ANSWER 41 OF 43 CAPLUS COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 1992:490312 CAPLUS Full-text  
 DOCUMENT NUMBER: 117:90312  
 ORIGINAL REFERENCE NO.: 117:15773a,15776a  
 TITLE: Preparation of xanthine derivatives as  
 antiasthmatics  
 and agents for treating osteoporosis  
 INVENTOR(S): Suzuki, Fumio; Shimada, Junichi; Ishii, Akio;  
 Nonaka,  
 Hiromi; Kosaka, Nobuo; Ichikawa, Shunji  
 PATENT ASSIGNEE(S): Kyowa Hakko Kogyo Co., Ltd., Japan  
 SOURCE: PCT Int. Appl., 48 pp.  
 CODEN: PIXXD2  
 DOCUMENT TYPE: Patent  
 LANGUAGE: Japanese  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9206976	A1	19920430	WO 1991-JP1420	
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RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LU, NL, SE				
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CA 2094270	C	19970121		
EP 559893	A1	19930915	EP 1991-917824	
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EP 559893	B1	19990203		
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JP 2843671	B2	19990106	JP 1991-516529	
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AT 176470	T	19990215	AT 1991-917824	
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ES 2130138	T3	19990701	ES 1991-917824	
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US 5756735	A	19980526	US 1995-483159	
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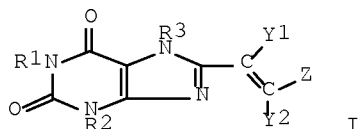
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US 1993-39193 B1

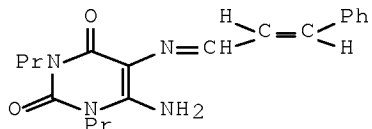
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OTHER SOURCE(S): CASREACT 117:90312; MARPAT 117:90312

GI



I



II

AB Xanthine derivs. [I, R1, R2 = H, Pr, Bu, allyl; R3 = H, alkyl; Y1, Y2 = H, Me, Z = (substituted) Ph, pyridyl, imidazolyl, furyl, thienyl], effective adenosine antagonists, are prepared and formulated. Condensation reaction of cinnamaldehyde with 5,6-diamino-1,3-dipropyluracil in MeOH-HOAc gave 70% enamine II, which was refluxed with FeCl3 in EtOH to give 61% (E)-I (R1 = R2 = Pr, R3 = Y2 = Y2 = H, Z = Ph) (III). Methylation of III with MeI in DMF gave 84% (E)-I (R3 = Me, others remain unchanged) which showed 82% inhibition of adenosine A1 receptor and 96% inhibition of A2 receptor at 10-4 M. I also showed 119% inhibition of bone absorption.

II Preparation of xanthine derivatives as antiasthmatics and agents for

treating osteoporosis

REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS

RECORD. ALL CITATIONS AVAILABLE IN THE

RE FORMAT

PI WO 9206976 A1 19920430

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
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PI WO 9206976	A1	19920430	WO 1991-JP1420	
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W: CA, JP, US

RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LU, NL, SE

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EP 559893	A1	19930915	EP 1991-917824	
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EP 559893	B1	19990203		
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R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE

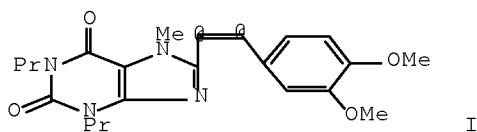
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 142665-37-0P  
     142665-38-1P  
     RL: SPN (Synthetic preparation); PREP (Preparation)  
         (preparation of, as antiasthmatic and antiosteoporosis agent)

L21 ANSWER 42 OF 43 CAPLUS COPYRIGHT 2009 ACS on STN  
 ACCESSION NUMBER:            1992:419919 CAPLUS Full-text  
 DOCUMENT NUMBER:            117:19919  
 ORIGINAL REFERENCE NO.:    117:3417a,3420a  
 TITLE:                        (E)-1,3-Dialkyl-7-methyl-8-(3,4,5-trimethoxystyryl)xanthines: potent and selective adenosine A2 antagonists  
 AUTHOR(S):                   Shimada, Junichi; Suzuki, Fumio; Nonaka, Hiromi;  
                                  Ishii, Akio; Ichikawa, Shunji  
 CORPORATE SOURCE:           Pharm. Res. Lab., Kyowa Hakko Kogyo Co., Ltd., Nagaizumicho, Japan  
 SOURCE:                        Journal of Medicinal Chemistry (1992), 35(12), 2342-5  
                                  CODEN: JMCMAR; ISSN: 0022-2623  
 DOCUMENT TYPE:                Journal  
 LANGUAGE:                      English  
 GI



AB    A series of 8-substituted 1,3,7-trialkylxanthines was tested for their hydrophobic interactions with the adenosine A2 receptor. (E)-Styryl substitution at the 8-position increased the affinity at the A2 receptor and A2 selectivity. Furthermore introduction of dimethoxy or trimethoxy group into the 8-styryl substituent of

1,3-dipropyl-7-methylxanthines enhanced the A2 selectivity in general. No apparent differences in the affinity at the A2 receptor were observed among a series of (E)-1,3-dialkyl-7-methyl-8-(3,5,6-trimethoxystyryl)xanthine derivs. This result is greatly contrasting with that of 1,3-disubstituted 8-alkyl- or 8-polycycloalkylxanthine derivs. where 1,3-disubstituents dramatically influenced affinity at the A1 receptor and its selectivity. The most potent A2 antagonist, (E)-1,3-dipropyl-7-methyl-8-(3,4-dimethoxystyryl)xanthine (I) ( $K_i = 7.8$  nM, A1/A2 = 190) produced a much larger shift of the NECA dose-response curve for blood pressure (A2) than for heart rate (A1) at the oral dose of 30 mg/kg.

TI (E)-1,3-Dialkyl-7-methyl-8-(3,4,5-trimethoxystyryl)xanthines:  
potent and

selective adenosine A2 antagonists

SO Journal of Medicinal Chemistry (1992), 35(12), 2342-5  
CODEN: JMCMAR; ISSN: 0022-2623

IT 120362-53-0 132940-39-7 132940-42-2 141807-86-5 141807-87-  
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7  
141824-00-2 141824-01-3

RL: BAC (Biological activity or effector, except adverse); BSU  
(Biological  
study, unclassified); BIOL (Biological study)  
(adenosine A2 receptor antagonist activity of)

L21 ANSWER 43 OF 43 CAPLUS COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 1974:40984 CAPLUS Full-text  
DOCUMENT NUMBER: 80:40984  
ORIGINAL REFERENCE NO.: 80:6687a,6690a  
TITLE: Photo-induced isomerization of  
8-(3,4,5-trimethoxystyryl)caffeine as possible  
route  
of drug decomposition

AUTHOR(S): Philip, Jose; Szulczewski, Dale H.  
CORPORATE SOURCE: Pharm. Res. Dev. Dep., Parke, Davis and Co.,  
Detroit,

MI, USA  
SOURCE: Journal of Pharmaceutical Sciences (1973),  
62(11), 1885-7  
CODEN: JPMSAE; ISSN: 0022-3549

DOCUMENT TYPE: Journal

LANGUAGE: English

AB trans-8-(3,4,5-Trimethoxystyryl)caffeine, dissolved in MeOH or  
CHCl3 rapidly isomerizes to an equilibrium mixture of trans-cis-  
isomers in the presence of visible light. Geometric isomerization  
was estimated by catalytic hydrogenation of both reactant and  
product to yield 8-(3,4,5-trimethoxyphenethyl)caffeine.

TI Photo-induced isomerization of 8-(3,4,5-trimethoxystyryl)caffeine  
as  
possible route of drug decomposition

SO Journal of Pharmaceutical Sciences (1973), 62(11), 1885-7  
CODEN: JPMSAE; ISSN: 0022-3549

IT 51389-37-8  
RL: PROC (Process)  
(photoisomerization of)

<http://www.cas.org/support/stngen/stdoc/properties.html>

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E2	1	155270-98-7/RN
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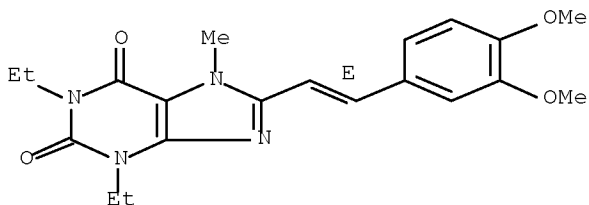
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L7 ANSWER 1 OF 1 REGISTRY COPYRIGHT 2009 ACS on STN  
RN 155270-99-8 REGISTRY  
ED Entered STN: 24 May 1994  
CN 1H-Purine-2,6-dione, 8-[(1E)-2-(3,4-dimethoxyphenyl)ethenyl]-1,3-diethyl-3,7-dihydro-7-methyl- (CA INDEX NAME)  
OTHER CA INDEX NAMES:  
CN 1H-Purine-2,6-dione, 8-[2-(3,4-dimethoxyphenyl)ethenyl]-1,3-diethyl-3,7-dihydro-7-methyl-, (E)-  
OTHER NAMES:  
CN Istradefylline  
CN KW 6002  
FS STEREOSEARCH  
MF C20 H24 N4 O4  
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SR CA  
LC STN Files: ADISINSIGHT, ADISNEWS, AGRICOLA, BIOSIS, BIOTECHNO, CA, CAPLUS, CASREACT, CBNB, CHEMCATS, CIN, EMBASE, IMSPATENTS, IMSRESEARCH, IPA, MEDLINE, PHAR, PROMT, PROUSDDR, RTECS\*, SYNTHLINE, TOXCENTER, USAN, USPAT2, USPATFULL  
(\*File contains numerically searchable property data)

Double bond geometry as shown.



\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

103 REFERENCES IN FILE CA (1907 TO DATE)

104 REFERENCES IN FILE CAPLUS (1907 TO DATE)

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E14	1	ISTOPIRIN/CN
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E24	1	ISURETIN/CN

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L8 1 ISTRADefYLLINE/CN

=> d l8

L8 ANSWER 1 OF 1 REGISTRY COPYRIGHT 2009 ACS on STN

RN 155270-99-8 REGISTRY

ED Entered STN: 24 May 1994

CN 1H-Purine-2,6-dione, 8-[(1E)-2-(3,4-dimethoxyphenyl)ethenyl]-1,3-diethyl-

3,7-dihydro-7-methyl- (CA INDEX NAME)

OTHER CA INDEX NAMES:

CN 1H-Purine-2,6-dione, 8-[2-(3,4-dimethoxyphenyl)ethenyl]-1,3-diethyl-3,7-

dihydro-7-methyl-, (E)-

OTHER NAMES:

CN Istradefylline

CN KW 6002

FS STEREOSEARCH

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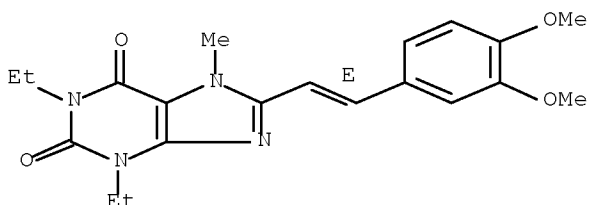
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LC STN Files: ADISINSIGHT, ADISNEWS, AGRICOLA, BIOSIS, BIOTECHNO,

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 IPA, MEDLINE, PHAR, PROMT, PROUSDDR, RTECS\*, SYNTHLINE,  
 TOXCENTER, USAN,  
 USPAT2, USPATFULL  
 (\*File contains numerically searchable property data)

Double bond geometry as shown.



\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

103 REFERENCES IN FILE CA (1907 TO DATE)  
 104 REFERENCES IN FILE CAPLUS (1907 TO DATE)

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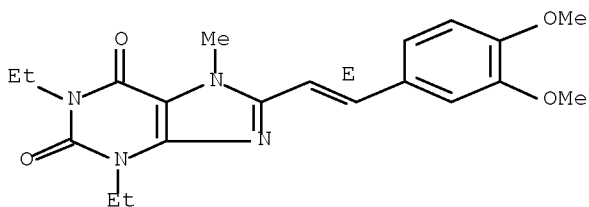
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L9 ANSWER 1 OF 1 REGISTRY COPYRIGHT 2009 ACS on STN  
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IPA, MEDLINE, PHAR, PROMT, PROUSDDR, RTECS\*, SYNTHLINE,  
TOXCENTER, USAN,  
USPAT2, USPATFULL  
(\*File contains numerically searchable property data)

Double bond geometry as shown.



<http://www.cas.org/legal/infopolicy.html>

This file contains CAS Registry Numbers for easy and accurate substance identification.

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L13 ANSWER 1 OF 28 CAPLUS COPYRIGHT 2009 ACS on STN  
ACCESSION NUMBER: 2006:579608 CAPLUS Full-text  
DOCUMENT NUMBER: 145:40296  
TITLE: Adenosine A2a receptor antagonists  
for the treatment of extra-pyramidal syndrome  
and  
other movement disorders  
INVENTOR(S): Grzelak, Michael; Hunter, John; Pond,  
Annamarie;  
Varty, Geoffrey  
PATENT ASSIGNEE(S): USA  
SOURCE: U.S. Pat. Appl. Publ., 28 pp., Cont.-in-part  
of U.S.  
Ser. No. 234,644.  
CODEN: USXXCO  
DOCUMENT TYPE: Patent  
LANGUAGE: English  
FAMILY ACC. NUM. COUNT: 3  
PATENT INFORMATION:

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EP 2001511 A1 20081217 EP 2006-825743  
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MX 2008004876 A 20080625 MX 2008-4876

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NO 2008002175 A 20080711 NO 2008-2175

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CN 101325974 A 20081217 CN 2006-80046347

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PRIORITY APPLN. INFO.: US 2002-435321P P  
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US 2003-738906 A2  
20031217

US 2005-234644 A2  
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CN 2003-80107087 A3  
20031217

WO 2003-US40456 W  
20031217

US 2005-249796 A  
20051013

WO 2006-US39689 W  
20061011

OTHER SOURCE(S): MARPAT 145:40296

AB A method for the treatment or prevention of extra pyramidal  
syndrome (EPS), dystonia, restless legs syndrome (RLS) or periodic  
leg movement in sleep (PLMS) comprising the administration of an  
adenosine A2a receptor antagonist, alone or in combination with  
other agents is described. Pharmaceutical compns. consisting of  
an adenosine A2a receptor antagonist in combination with an  
antipsychotic agent, an anticonvulsant agent, lithium or an opioid

are also provided. Thus, monkeys, previously sensitized to the chronic effects of haloperidol, that exhibited EPS when administered haloperidol acutely, were used in a crossover, balanced design study to evaluate adenosine A2a receptor antagonist administered orally, in conjunction with haloperidol. The adenosine A2a receptor antagonist studied prevented the onset of EPS and delayed the onset of EPS by an average of 2.3 to 2.9 h.

- TI Adenosine A2a receptor antagonists for the treatment of extra-pyramidal syndrome and other movement disorders
- TI Adenosine A2a receptor antagonists for the treatment of extra-pyramidal syndrome and other movement disorders

L13 ANSWER 2 OF 28 CAPLUS COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 2006:463565 CAPLUS Full-text

DOCUMENT NUMBER: 144:460860

TITLE: Adenosine A2a receptor antagonists for the treatment of extrapyramidal syndrome

and other

movement disorders

INVENTOR(S): Grzelak, Michael; Hunter, John; Pond, Annamarie;

Varty, Geoffrey

PATENT ASSIGNEE(S): USA

SOURCE: U.S. Pat. Appl. Publ., 27 pp., Cont.-in-part of U.S.

Ser. No. 738,906.

CODEN: USXXCO

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 3

PATENT INFORMATION:

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OTHER SOURCE(S): MARPAT 144:460860

AB The invention discloses a method for the treatment or prevention of extrapyramidal syndrome (EPS), dystonia, restless legs syndrome (RLS) or periodic leg movement in sleep (PLMS), comprising the administration of an adenosine A2a receptor antagonist, alone or in combination with other agents useful for treating EPS, dystonia, RLS or PLMS.

TI Adenosine A2a receptor antagonists for the treatment of extrapyramidal syndrome and other movement disorders

TI Adenosine A2a receptor antagonists for the treatment of extrapyramidal syndrome and other movement disorders

L13 ANSWER 3 OF 28 CAPLUS COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 2004:203674 CAPLUS Full-text

DOCUMENT NUMBER: 140:229467

TITLE: Adenosine A2A receptor antagonists for treating restless legs syndrome or related disorders

INVENTOR(S): Kase, Hiroshi; Seno, Naoki; Mori, Akihisa; Zhao, Dayao

PATENT ASSIGNEE(S): Kyowa Hakko Kogyo Co. Ltd., Japan

SOURCE: PCT Int. Appl., 54 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

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WO 2004019949	A1	20040311	WO 2003-US26644	
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L13 ANSWER 4 OF 28 CAPLUS COPYRIGHT 2009 ACS on STN  
ACCESSION NUMBER: 2003:610271 CAPLUS Full-text  
DOCUMENT NUMBER: 139:143978  
TITLE: Methods using adenosine A2A receptor  
antagonists for treating Parkinson's disease  
patients suffering from L-DOPA/dopamine  
agonist  
therapy-associated movement disorders  
INVENTOR(S): Kase, Hiroshi; Mori, Akihisa; Waki, Yutaka;  
Ohsawa,  
Yutaka; Karasawa, Akira; Kuwana, Yoshitoshi  
PATENT ASSIGNEE(S): Japan  
SOURCE: PCT Int. Appl., 95 pp.  
CODEN: PIXXD2  
DOCUMENT TYPE: Patent  
LANGUAGE: English  
FAMILY ACC. NUM. COUNT: 1  
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
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 OTHER SOURCE(S):                    MARPAT 139:143978

AB The invention provides methods for treating movement disorders by administering an effective amount of one or more adenosine A2A receptor antagonist(s) to a patient in need thereof. The invention also provides methods of decreasing the adverse effects of L-DOPA in patients receiving L-DOPA therapy in the treatment of Parkinson's disease. The invention further provides methods and compns. for treating Parkinson's disease patients with sub-clin. EDs of L-DOPA by combining L-DOPA treatment with an effective amount of one or more adenosine A2A receptor antagonists (i.e., L-DOPA sparing effect). The invention further provides methods of effective treatment of Parkinson's disease by co-administering at least one adenosine A2A receptor antagonist, L-DOPA, and a dopamine agonist and/or a COMT inhibitor and/or a MAO inhibitor. The invention further provides methods of prolonging effective treatment of Parkinson's disease by administering an adenosine A2A receptor antagonist singly or together with a dopamine agonist, and/or a COMT inhibitor, and/or a MAO inhibitor without prior or subsequent administration of L-DOPA, delaying or removing onset of L-DOPA motor complication.

TI Methods using adenosine A2A receptor antagonists for treating Parkinson's disease patients suffering from L-DOPA/dopamine

agonist therapy-associated movement disorders

REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS

RECORD. ALL CITATIONS AVAILABLE IN THE

RE FORMAT

TI Methods using adenosine A2A receptor antagonists for treating Parkinson's disease patients suffering from L-DOPA/dopamine

agonist therapy-associated movement disorders

PRAI US 2002-352413P P 20020128 <--  
AU 2003-207734 A3 20030128  
US 2003-353240 A3 20030128  
WO 2003-US2658 W 20030128

AB The invention provides methods for treating movement disorders by administering an effective amount of one or more adenosine A2A receptor antagonist(s) to a patient in need thereof. The invention also provides methods of decreasing the adverse effects of L-DOPA in patients receiving L-DOPA therapy in the treatment of Parkinson's disease. The invention further provides methods and compns. for treating Parkinson's disease patients with sub-clin. EDs of L-DOPA by combining L-DOPA treatment with an effective amount of one or more adenosine A2A receptor antagonists (i.e., L-DOPA sparing effect). The invention further provides methods of effective treatment of Parkinson's disease by co-administering at least one adenosine A2A receptor antagonist, L-DOPA, and a dopamine agonist and/or a COMT inhibitor and/or a MAO inhibitor. The invention further provides methods of prolonging effective treatment of Parkinson's disease by administering an adenosine A2A receptor antagonist singly or together with a dopamine agonist, and/or a COMT inhibitor, and/or a MAO inhibitor without prior or subsequent administration of L-DOPA, delaying or removing onset of L-DOPA motor complication.

ST DOPA motor complication Parkinson drug adenosine A2a antagonist; dopamine agonist motor complication Parkinson drug adenosine A2a antagonist

IT Purinoceptor antagonists  
 (A2; adenosine A2a antagonist for treating  
 Parkinson's disease patients with L-DOPA/dopamine agonist  
 therapy-associated motor complications)

IT Adenosine receptors  
 RL: BSU (Biological study, unclassified); BIOL (Biological study)  
 (A2A; adenosine A2a antagonist for treating  
 Parkinson's disease patients with L-DOPA/dopamine agonist  
 therapy-associated motor complications)

L13 ANSWER 5 OF 28 CAPLUS COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 2003:472597 CAPLUS Full-text

DOCUMENT NUMBER: 139:47145

TITLE: Methods for using extracellular adenosine  
 inhibitors and adenosine receptor inhibitors  
 to enhance immune response and inflammation

INVENTOR(S): Sitkovsky, Michail V.; Ohta, Akio

PATENT ASSIGNEE(S): The Government of the United States of America  
 as  
 Represented by the Secretary, Department of  
 Health and  
 Human Services, USA

SOURCE: PCT Int. Appl., 60 pp.  
 CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003050241	A2	20030619	WO 2002-US36829	
20021114 <--				
WO 2003050241	A3	20040129		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA,				
CH, CN,				
CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD,				
GE, GH,				
GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC,				
LK, LR,				
LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ,				
OM, PH,				
PL, PT, RO, RU, SC, SD, SE, SG, SI, SK, SL, TJ, TM, TN,				
TR, TT,				
TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM,				
AZ, BY,				
KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK,				
EE, ES,				
FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF,				
BJ, CF,				
CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2470104	A1	20030619	CA 2002-2470104	
20021114 <--				

AU 2002356962	A1	20030623	AU 2002-356962
20021114 <--			
EP 1465634	A2	20041013	EP 2002-804693
20021114 <--			
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,			
IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK			
JP 2005516917	T	20050609	JP 2003-551263
20021114 <--			
US 20050220799	A1	20051006	US 2004-498416
20040610 <--			
PRIORITY APPLN. INFO.:			US 2001-340772P P
20011212 <--			US 2001-342585P P
20011219 <--			WO 2002-US36829 W
20021114 <--			
AB	A method is provided to increase an immune response to an antigen. The method includes administering an agent that inhibits extracellular adenosine or inhibits adenosine receptors. Also disclosed are methods to increase the efficacy of a vaccine and to increase an immune response to a tumor antigen or immune cell-mediated tumor destruction.		
TI	Methods for using extracellular adenosine inhibitors and adenosine receptor inhibitors to enhance immune response and inflammation		

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L13 ANSWER 6 OF 28 CAPLUS COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER:	2003:135720 CAPLUS <u>Full-text</u>
DOCUMENT NUMBER:	139:239332
TITLE:	Adenosine A <sub>2A</sub> receptor antagonists-A novel approach to therapeutic drug for parkinsonism
AUTHOR(S):	Kase, Hiroshi
CORPORATE SOURCE:	Kyowa Hakko Kogyo Co., Ltd., Tokyo, Chiyoda, Ohtemachi, 100-8185, Japan
SOURCE:	Seitai no Kagaku (2002), 53(6), 592-600 CODEN: SEKAA6; ISSN: 0370-9531
PUBLISHER:	Kanehara Ichiro Kinen Igaku Iryo Shinko Zaidan
DOCUMENT TYPE:	Journal; General Review
LANGUAGE:	Japanese
AB	A review, discussing the action mechanism and clin. pharmacol. of adenosine A <sub>2A</sub> receptor antagonists, including KW 6002 for treatment of parkinsonism.
TI	Adenosine A <sub>2A</sub> receptor antagonists-A novel approach to therapeutic drug for parkinsonism
TI	Adenosine A <sub>2A</sub> receptor antagonists-A novel approach to therapeutic drug for parkinsonism
SO	Seitai no Kagaku (2002), 53(6), 592-600 CODEN: SEKAA6; ISSN: 0370-9531
AB	A review, discussing the action mechanism and clin. pharmacol. of adenosine A <sub>2A</sub> receptor antagonists, including KW 6002 for treatment of parkinsonism.
ST	review adenosine A <sub>2A</sub> receptor antagonists

antagonist parkinsonism

IT Adenosine receptors  
 RL: BSU (Biological study, unclassified); BIOL (Biological study)  
 (A2; adenosine A $\downarrow$ 2 $\downarrow$ A receptor  
 antagonists-A novel approach to therapeutic drug for  
 parkinsonism)

IT Antiparkinsonian agents  
 Human  
 Parkinson's disease  
 (adenosine A $\downarrow$ 2 $\downarrow$ A receptor antagonists  
 -A novel approach to therapeutic drug for parkinsonism)

IT 155270-99-8, KW 6002  
 RL: DMA (Drug mechanism of action); THU (Therapeutic use); BIOL  
 (Biological study); USES (Uses)  
 (adenosine A $\downarrow$ 2 $\downarrow$ A receptor antagonists  
 -A novel approach to therapeutic drug for parkinsonism)

L13 ANSWER 7 OF 28 CAPLUS COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 2002:793451 CAPLUS Full-text

DOCUMENT NUMBER: 137:289033

TITLE: Adenosine A2A receptor antagonists  
 combined with neurotrophic activity compounds

in the

INVENTOR(S): treatment of Parkinson's disease  
 Peters, Dan; Ronn, Lars Christian; Nielsen,  
 Karin

PATENT ASSIGNEE(S): Sandager  
 Neurosearch A/S, Den.  
 SOURCE: PCT Int. Appl., 30 pp.  
 CODEN: PIXXD2

DOCUMENT TYPE: Patent  
 LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002080957	A1	20021017	WO 2002-DK228	
20020404 <--				
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW			
RW:	GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN,			

TD, TG  
CA 2440196 A1 20021017 CA 2002-2440196  
20020404 <--  
AU 2002338309 A1 20021021 AU 2002-338309  
20020404 <--  
EP 1379269 A1 20040114 EP 2002-759761  
20020404 <--  
EP 1379269 B1 20090304  
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE,  
MC, PT,  
IE, SI, LT, LV, FI, RO, MK, CY, AL, TR  
JP 2004529916 T 20040930 JP 2002-578996  
20020404 <--  
US 20040097540 A1 20040520 US 2003-473809  
20031002 <--  
US 7160899 B2 20070109  
MX 2003009185 A 20040217 MX 2003-9185  
20031008 <--  
PRIORITY APPLN. INFO.: DK 2001-583 A  
20010409 <--  
WO 2002-DK228 W  
20020404 <--  
AB This invention relates to the use of the combined action of a  
compound with neurotrophic activity and an adenosine A2A receptor  
antagonist for the treatment of Parkinson's disease. Adenosine A2A  
receptor antagonist is selected from the group consisting of KW-  
6002, ZM-241385, 8FB-PTP, SCH-58261, KF-17837, CGS-15943, DMPX,  
and pharmaceutically acceptable salts thereof. A compound with  
neurotrophic activity is selected from the group consisting of 5-  
(4-Chlorophenyl)-8-methyl-6,7,8,9-tetrahydro-1H-pyrrolo[3,2-  
h]isoquinoline-2,3-dione-3-oxime; 5-(4-Chlorophenyl)-6,7,8,9-  
tetrahydro-1H-pyrrolo[3,2-h]naphthalene-2,3-dione-3-oxime; GDNF;  
Neublastin; and pharmaceutically acceptable salts thereof.  
TI Adenosine A2A receptor antagonists combined with  
neurotrophic activity compounds in the treatment of Parkinson's  
disease  
REFERENCE COUNT: 11 THERE ARE 11 CITED REFERENCES AVAILABLE  
FOR THIS  
RECORD. ALL CITATIONS AVAILABLE IN THE  
RE FORMAT  
TI Adenosine A2A receptor antagonists combined with  
neurotrophic activity compounds in the treatment of Parkinson's  
disease  
PI WO 2002080957 A1 20021017  
PATENT NO. KIND DATE APPLICATION NO. DATE  
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PI WO 2002080957 A1 20021017 WO 2002-DK228  
20020404 <--  
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA,  
CH, CN,  
CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD,  
GE, GH,  
GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC,  
LK, LR,  
LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ,  
OM, PH,

PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR,  
 TT, TZ,  
 UA, UG, US, UZ, VN, YU, ZA, ZM, ZW  
 RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT,  
 BE, CH,  
 CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT,  
 SE, TR,  
 BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN,  
 TD, TG

CA 2440196 A1 20021017 CA 2002-2440196

20020404 <--

AU 2002338309 A1 20021021 AU 2002-338309

20020404 <--

EP 1379269 A1 20040114 EP 2002-759761

20020404 <--

EP 1379269 B1 20090304

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE,  
 MC, PT,

IE, SI, LT, LV, FI, RO, MK, CY, AL, TR

JP 2004529916 T 20040930 JP 2002-578996

20020404 <--

US 20040097540 A1 20040520 US 2003-473809

20031002 <--

US 7160899 B2 20070109

MX 2003009185 A 20040217 MX 2003-9185

20031008 <--

PRAI DK 2001-583 A 20010409 <--

WO 2002-DK228 W 20020404 <--

AB This invention relates to the use of the combined action of a compound with neurotrophic activity and an adenosine A2A receptor antagonist for the treatment of Parkinson's disease. Adenosine A2A receptor antagonist is selected from the group consisting of KW-6002, ZM-241385, 8FB-PTP, SCH-58261, KF-17837, CGS-15943, DMPX, and pharmaceutically acceptable salts thereof. A compound with neurotrophic activity is selected from the group consisting of 5-(4-Chlorophenyl)-8-methyl-6,7,8,9-tetrahydro-1H-pyrrolo[3,2-h]isoquinoline-2,3-dione-3-oxime; 5-(4-Chlorophenyl)-6,7,8,9-tetrahydro-1H-pyrrolo[3,2-h]naphthalene-2,3-dione-3-oxime; GDNF; Neublentin; and pharmaceutically acceptable salts thereof.

ST adenosine receptor antagonist neurotrophic Parkinson disease antiparkinsonian

IT Purinoceptor antagonists

(A2; adenosine A2A receptor antagonists combined with neurotrophic compds. in treatment of Parkinson's disease)

L13 ANSWER 8 OF 28 CAPLUS COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 2002:787693 CAPLUS Full-text

DOCUMENT NUMBER: 138:314421

TITLE: Distribution of adenosine A2A receptor antagonist KW-6002 and its effect on gene expression in the rat brain

AUTHOR(S): Aoyama, Shiro; Koga, Kumiko; Mori, Akihisa; Miyaji,

Hiromasa; Sekine, Susumu; Kase, Hiroshi; Uchimura,

CORPORATE SOURCE: Tatsuo; Kobayashi, Hiroyuki; Kuwana, Yoshihisa  
Pharmaceutical Res. Inst., Kyowa Hakko Kogyo  
Co. Ltd.,

SOURCE: Sunto-gun, Shizuoka, 411-8731, Japan  
Brain Research (2002), 953(1,2), 119-125  
CODEN: BRREAP; ISSN: 0006-8993

PUBLISHER: Elsevier Science B.V.

DOCUMENT TYPE: Journal

LANGUAGE: English

AB A novel adenosine A2A receptor selective antagonist, KW-6002 [(E)-1,3-diethyl-8-(3,4-dimethoxystyryl)-7-methyl-3,7-dihydro-1H-purine-2,6-dione], possesses antiparkinsonian activities in rodent and primate models. In the present study, the authors investigated the distribution of [<sup>14</sup>C]KW-6002 in forebrain after oral administration at pharmacol. EDs. Also, the authors monitored the effects of the compound on preproenkephalin (PPE) and preprotachykinin (PPT) gene expression in rat striatum. The highest level of radioactivity was observed in the striatum after oral administration of [<sup>14</sup>C]KW-6002; 30 min after 0.1 and 0.3 mg/kg, the d. values in the striatum were 2.45 and 2.43 times higher than those in a reference region (frontal cortex), resp. At the dose of 3 mg/kg, p.o., the ratio was only 1.58 and the compound was distributed more extensively in the brain. The distribution pattern and intensity of radioactivity were maintained even 90 min after the administration of [<sup>14</sup>C]KW-6002. Oral administration of KW-6002 (0.3 and 3 mg/kg/day) to rats for 14 days reversed the increased gene expression of PPE in striatum that had been depleted of dopamine by prior treatment with 6-hydroxydopamine (6-OHDA). On the other hand, KW-6002 did not alter the decreased gene expression of PPT in 6-OHDA-treated rats. These results are the 1st to show directly that orally administered KW-6002 is distributed selectively to the striatum and that it modulates the activity of striatopallidal enkephalin-containing neurons but not striatonigral substance P-containing neurons.

TI Distribution of adenosine A2A receptor antagonist  
KW-6002 and its effect on gene expression in the rat brain

L13 ANSWER 9 OF 28 CAPLUS COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 2002:90903 CAPLUS Full-text

DOCUMENT NUMBER: 136:277364

TITLE: Neuroprotection by adenosine A2A receptor  
blockade in experimental models of Parkinson's

disease

AUTHOR(S): Ikeda, Ken; Kurokawa, Masako; Aoyama, Shiro;  
Kuwana,

Yoshihisa  
CORPORATE SOURCE: Pharmaceutical Research Institute, Kyowa Hakko  
Kogyo

Co., Ltd., Shizuoka, 411-8731, Japan  
SOURCE: Journal of Neurochemistry (2002), 80(2),  
262-270

CODEN: JONRA9; ISSN: 0022-3042

PUBLISHER: Blackwell Publishing Ltd.

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Adenosine A2A receptors are abundant in the caudate-putamen and involved in the motor control in several species. In MPTP-treated monkeys, A2A receptor-blockade with an antagonist alleviates parkinsonian symptoms without provoking dyskinesia, suggesting this receptor may offer a new target for the antisymptomatic therapy of Parkinson's disease. In the present study, a significant neuroprotective effect of A2A receptor antagonists is shown in exptl. models of Parkinson's disease. Oral administration of A2A receptor antagonists protected against the loss of nigral dopaminergic neuronal cells induced by 6-hydroxydopamine in rats. A2A antagonists also prevented the functional loss of dopaminergic nerve terminals in the striatum and the ensuing gliosis caused by MPTP in mice. The neuroprotective property of A2A receptor antagonists may be exerted by altering the packaging of these neurotoxins into vesicles, thus reducing their effective intracellular concentration. We therefore conclude that the adenosine A2A receptor may provide a novel target for the long-term medication of Parkinson's disease, because blockade of this receptor exerts both acutely antisymptomatic and chronically neuroprotective activities.

TI Neuroprotection by adenosine A2A receptor blockade in experimental models of Parkinson's disease

REFERENCE COUNT: 48 THERE ARE 48 CITED REFERENCES AVAILABLE FOR THIS

RECORD. ALL CITATIONS AVAILABLE IN THE

RE FORMAT

TI Neuroprotection by adenosine A2A receptor blockade in experimental models of Parkinson's disease

L13 ANSWER 10 OF 28 CAPLUS COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 2002:943 CAPLUS Full-text

DOCUMENT NUMBER: 137:88308

TITLE: Adenosine A2A receptor antagonists  
: Potential therapeutic and neuroprotective effects in

Parkinson's disease

AUTHOR(S): Morelli, M.; Wardas, J.

CORPORATE SOURCE: Department of Toxicology, University of Cagliari,

Palazzo delle Scienze, Cagliari, 09124, Italy

SOURCE: Neurotoxicity Research (2001), 3(6), 545-556

CODEN: NURRFI; ISSN: 1029-8428

PUBLISHER: Harwood Academic Publishers

DOCUMENT TYPE: Journal

LANGUAGE: English

AB The most effective treatment of Parkinson's disease (PD) is, at present, the dopamine precursor L-3,4-dihydroxyphenyl-alanine (L-DOPA), however a number of disadvantages such as a loss of drug efficacy and severe side-effects (psychoses, dyskinesias and on-off phenomena) limit long-term, effective utilization of this drug. Recent exptl. studies in which selective antagonists of adenosine A2A receptors were used, have shown an improvement in motor disabilities in animal models of PD. The A2A antagonist

[7-(2-phenylethyl)-5-amino-2-(2-furyl)-pyrazolo-(4,3-e)-1,2,4-triazolo(1,5- c)pyrimidine] (SCH 58261) potentiated the contralateral turning behavior induced by a threshold dose of L-DOPA or direct dopamine receptor agonists in unilaterally 6-hydroxydopamine (6-OHDA) lesioned rats, an effect accompanied by an increase in Foslike-immunoreactivity in neurons of the lesioned striatum. Likewise, other A2A receptor antagonists such as (3,7-dimethyl-1-propargylxanthine) (DMPX), [E-8-(3,4-dimethoxystyryl)-1,3-dipropyl-7-methylxanthine] (KF 17837) and [E-1,3-diethyl-8-(3,4-dimethoxystyryl)-7-methyl-3,7-dihydro-1H-purine-2, 6-dione] (KW 6002) antagonized catalepsy induced by haloperidol or reserpine in the rat, whereas in non-human primate models of PD, KW 6002 reduced the rigidity and improved the disability score of MPTP-treated marmosets and cynomolgus monkeys. Moreover, in contrast to L-DOPA, selective A2A receptor antagonists administered chronically did not produce dyskinesias and did not evoke tolerance in 6-OHDA and MPTP models of PD. An addnl. therapeutic potential of adenosine A2A antagonists emerged from studies showing neuroprotective properties of these compds. in animal models of cerebral ischemia and excitotoxicity, as well as in the (1-methyl-4-phenyl-1,2,3,6- tetrahydropyridine) (MPTP) model of PD. Adenosine A2A receptor antagonists by reversing motor impairments in animal models of PD and by contrasting cell degeneration are some of the most promising compds. for the treatment of PD.

TI Adenosine A2A receptor antagonists: Potential therapeutic and neuroprotective effects in Parkinson's disease

L13 ANSWER 11 OF 28 CAPLUS COPYRIGHT 2009 ACS on STN  
 ACCESSION NUMBER: 2001:915602 CAPLUS Full-text  
 DOCUMENT NUMBER: 136:303408  
 TITLE: New developments in A1 and A2 adenosine receptor antagonists  
 AUTHOR(S): Kiec-Kononowicz, K.; Drabczynska, A.; Pekala, E.;  
 Michalak, B.; Miller, C. E.; Schumacher, B.; Karolak-Wojciechowska, J.; Duddeck, H.;  
 Rockitt, S.;  
 Wartchow, R.  
 CORPORATE SOURCE: IUPAC Commission, Medical College, Department of  
 Chemical Technology of Drugs, Jagiellonian  
 University,  
 Krakow, PL 30-688, Pol.  
 SOURCE: Pure and Applied Chemistry (2001), 73(9), 1411-1420  
 CODEN: PACHAS; ISSN: 0033-4545  
 PUBLISHER: International Union of Pure and Applied Chemistry  
 DOCUMENT TYPE: Journal; General Review  
 LANGUAGE: English  
 AB A review with refs. The aim of this article is to briefly present progress in the development of the potent adenosine receptor (AR) antagonists with high selectivity for either A1, A2A or A2B ARs. The structural requirements for each AR subtype were discussed as well as their potential therapeutic use. In the search for new AR

antagonists. series of imidazo-, pyrimido-, and diazepino-purindione derivs. as well as oxazolo-, oxazino-, and oxazepino-purindiones were designed, synthesized, and preliminarily evaluated in pharmacol. studies. Oxygen-containing tricyclic derivs. were shown to be moderately potent AR antagonists exhibiting selectivity either for A1 or A2A ARs. Tricyclic purindiones with nitrogen in the third ring were generally more A2A AR selective. The compds. tested in vivo according to the Antiepileptic Drug Development Program of the National Institutes of Health (USA) were generally active as anticonvulsants in chemical induced seizures.

TI New developments in A1 and A2 adenosine receptor antagonists

L13 ANSWER 12 OF 28 CAPLUS COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 2001:910700 CAPLUS Full-text

DOCUMENT NUMBER: 136:31603

TITLE: Neuroprotection by caffeine and A2A adenosine receptor inactivation in a model of

Parkinson's

disease

AUTHOR(S): Chen, Jiang-Fan; Xu, Kui; Petzer, Jacobus P.; Staal,

Roland; Xu, Yue-Hang; Beilstein, Mark;

Sonsalla,

Patricia K.; Castagnoli, Kay; Castagnoli,

Neal, Jr.;

Schwarzschild, Michael A.

CORPORATE SOURCE: Molecular Neurobiology Laboratory, Department of

Neurology, Massachusetts General Hospital, Charlestown, MA, 02129, USA

SOURCE: Journal of Neuroscience (2001), 21(10), RC143/1-RC143/6

CODEN: JNRSDS; ISSN: 0270-6474

PUBLISHER: Society for Neuroscience

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Recent epidemiol. studies have established an association between the common consumption of coffee or other caffeinated beverages and a reduced risk of developing Parkinson's disease (PD). To explore the possibility that caffeine helps prevent the dopaminergic deficits characteristic of PD, we investigated the effects of caffeine and the adenosine receptor subtypes through which it may act in the 1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine (MPTP) neurotoxin model of PD. Caffeine, at doses comparable to those of typical human exposure, attenuated MPTP-induced loss of striatal dopamine and dopamine transporter binding sites. The effects of caffeine were mimicked by several A2A antagonists (7-(2-phenylethyl)-5-amino-2-(2-furyl)-pyrazolo-[4,3- e]-1,2,4-triazolo[1,5-c]pyrimidine (SCH 58261), 3,7-dimethyl-1-propargyl xanthine, and (E)-1,3-diethyl-8 (KW-6002)-(3,4-dimethoxystyryl)-7-methyl- 3,7-dihydro-1H-purine-2,6-dione) (KW-6002) and by genetic inactivation of the A2A receptor, but not by A1 receptor blockade with 8-cyclopentyl-1,3-dipropylxanthine,

suggesting that caffeine attenuates MPTP toxicity by A2A receptor blockade. These data establish a potential neural basis for the inverse association of caffeine with the development of PD, and they enhance the potential of A2A antagonists as a novel treatment for this neurodegenerative disease.

TI Neuroprotection by caffeine and A2A adenosine receptor inactivation in a model of Parkinson's disease

L13 ANSWER 13 OF 28 CAPLUS COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 2001:864519 CAPLUS Full-text

DOCUMENT NUMBER: 136:129190

TITLE: Solubilization and immunoprecipitation of rat striatal

adenosine A2A receptors

AUTHOR(S): Harvey, Victoria; Jones, Julie; Misra, Anil; Knight,

Antony R.; Quirk, Kathleen

CORPORATE SOURCE: Department of Molecular Pharmacology, Vernalis Research Ltd., Winnersh, Wokingham, RG41 5UA,

UK

SOURCE: European Journal of Pharmacology (2001), 431(2), 171-177

CODEN: EJPHAZ; ISSN: 0014-2999

PUBLISHER: Elsevier Science B.V.

DOCUMENT TYPE: Journal

LANGUAGE: English

AB In the present study, the authors have sought to solubilize adenosine A2A receptors from rat striatal membranes using a variety of different detergents. Of the detergents tested, 1% CHAPS yielded optimal conditions for solubilization (in the presence of 3 mg/mL protein, 44% of receptor was solubilized, 50% of total protein was solubilized). An antipeptide antibody was raised against a 15 amino-acid sequence within the predicted third intracellular loop region of the human and rat adenosine A2A receptor. The antibody was coupled to protein A immobilized on sepharose CL-4B and used to immunoppt. adenosine A2A receptors from solubilized rat striatal preps. Radioligand-binding studies were performed using the selective adenosine A2 antagonist [3H]ZM 241385. Using [3H]ZM 241385, the pharmacol. of immunopptd. adenosine A2A receptors was compared to striatal membrane bound adenosine A2A receptors and detergent solubilized adenosine A2A receptors. [H]ZM 241385 labeled a single saturable binding site with high affinity in all three preps. (membrane bound Kd 2.7 nM; solubilized Kd 1.9 nM; immunopptd. Kd 2.2 nM). Addnl., all three assays confirmed a rank order of potency for displacers consistent with adenosine A2A receptor pharmacol.: ZM 241385 > KW 6002 > CGS 21680 > DPCPX. The authors conclude that they have solubilized and immunopptd. adenosine A2A receptors from rat striatum and that their pharmacol. is consistent with native striatal adenosine A2A receptors.

TI Solubilization and immunoprecipitation of rat striatal adenosine A2A receptors

L13 ANSWER 14 OF 28 CAPLUS COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 2001:688889 CAPLUS Full-text  
DOCUMENT NUMBER: 136:48351  
TITLE: Adenosine A2A receptor antagonists  
are potential antidepressants: evidence based

on  
pharmacology and A2A receptor knockout mice  
AUTHOR(S): El Yacoubi, Malika; Ledent, Catherine;  
Parmentier,  
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AB Adenosine, an ubiquitous neuromodulator, and its analogs have been shown to produce "depressant" effects in animal models believed to be relevant to depressive disorders, while adenosine receptor antagonists have been found to reverse adenosine-mediated "depressant" effect. We have designed studies to assess whether adenosine A2A receptor antagonists, or genetic inactivation of the receptor would be effective in established screening procedures, such as tail suspension and forced swim tests, which are predictive of clin. antidepressant activity. Adenosine A2A receptor knockout mice were found to be less sensitive to "depressant" challenges than their wild-type littermates. Consistently, the adenosine A2A receptor blockers SCH 58261 (1-10 mg kg<sup>-1</sup>, i.p.) and KW 6002 (0.1-10 mg kg<sup>-1</sup>, p.o.) reduced the total immobility time in the tail suspension test. The efficacy of adenosine A2A receptor antagonists in reducing immobility time in the tail suspension test was confirmed and extended in two groups of mice. Specifically, SCH 58261 (1-10 mg kg<sup>-1</sup>) and ZM 241385 (15-60 mg kg<sup>-1</sup>) were effective in mice previously screened for having high immobility time, while SCH 58261 at 10 mg kg<sup>-1</sup> reduced immobility of mice that were selectively bred for their spontaneous "helplessness" in this assay. Addnl. expts. were carried out using the forced swim test. SCH 58261 at 10 mg kg<sup>-1</sup> reduced the immobility time by 61%, while KW 6002 decreased the total immobility time at the doses of 1 and 10 mg kg<sup>-1</sup> by 75 and 79%, resp. Administration of the dopamine D2 receptor antagonist haloperidol (50-200 µg kg<sup>-1</sup> i.p.) prevented the antidepressant-like effects elicited by SCH 58261 (10 mg kg<sup>-1</sup> i.p.) in forced swim test whereas it left unaltered its stimulant motor effects. In conclusion, these data support the hypothesis that A2A receptor antagonists prolong escape-directed behavior in two screening tests for antidepressants. Altogether the results support the hypothesis that blockade of the adenosine A2A receptor might be an interesting target for the development of effective antidepressant agents.

TI Adenosine A2A receptor antagonists are potential  
antidepressants: evidence based on pharmacology and A2A receptor  
knockout

mice